The 18th Annual Meeting of Infantile Seizure Society

# International Symposium on Acute Encephalopathy in Infancy and Its Related Disorders (ISAE2016)

# **PROGRAM & ABSTRACTS**



Organizer	Infantile Seizure Society (ISS)	
Endorsement from	International League Against Epilepsy (ILAE)	
	Japan Medical Association (JMA)	
	Asian & Oceanian Child Neurology Association (AOCNA)	
	Japan Epilepsy Society (JES)	
	Japanese Society of Child Neurology (JSCN)	



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# Messsage from the President of ISAE2016



Hideo Yamanouchi, MD President, ISAE2016



Masashi Mizuguchi, MD Vice-President, ISAE2016

Dear Friends and Colleagues:

It is an honor and privilege to offer a warm welcome to all of you who have traveled from all over the world to attend this International Symposium on Acute Encephalopathy in Infancy and Its Related Disorders (ISAE2016), held as the 18th Annual Meeting of Infantile Seizure Society (ISS). I would like to express sincere thanks for your attendance at this meeting.

We have prepared a very attractive scientific program comprising of 34 comprehensive reviews of recent scientific progress by invited experts in the field of acute encephalopathy and encephalitis in infancy. In addition, we have accepted 76 excellent abstracts for 31 platform and 45 poster presentations, all of which will no doubt make a significant contribution to the development of scientific research in these fields.

Both Professor Mizuguchi (Vice-President) and I sincerely hope that all of you explore this great opportunity to gain further insight into all fields of acute encephalopathy and encephalitis in infancy and to have fruitful discussions with each other.

山内参加

Hideo Yamanouchi, MD President, International Symposium on Acute Encephalopathy in Infancy and its Related Disorders (ISAE2016) Professor, Department of Pediatrics, Saitama Medical University

# Message from the Chairperson of Infantile Seizure Society



Dear Friends and Colleagues:

It is my great honor and pleasure to address my heartfelt welcome to all colleagues in the world who are willing to participate in the forthcoming International Symposium on Acute Encephalopathy/Encephalitis in Infancy and Its Related Disorders (ISAE) held as the 18<sup>th</sup> Annual Meeting of Infantile Seizure Society (ISS) under the endorsement of ILAE in Tokyo on July 1-3, 2016. Acute encephalopathy in infancy is frequently associated with prolonged seizures and/or comatose state, causing various degrees of neurological sequelae as well as intractable epilepsies. Thanks to the participation of the international experts that contributing to discussions of these advances on a number of important issue and hot topics, covering fields from a comprehensive review of recent advances in research and CME dealing with essential basics on acute encephalopathy/encephalitis in infancy. As you would acknowledge, acute encephalopathy/encephalitis in infancy are one of the most important subjects in child neurology which influence even morbidity and mortality. We sincerely hope that you will be able attend this appealing ISAE 2016 in Tokyo, in July, and to enrich your professional knowledge significantly. I am sure you will also enjoy an effectiveness of new plan, proposed by the previous president of ILAE Prof. Moshe, Educational Program for Leadership Development (Rehearsal Lessons by Experts)! In the great tradition of the spirit of the late Prof Fukuyama, the founder of ISS, our aim is to bring the participants together to discuss about the basic and clinical science of acute infantile encephalopathy/encephalitis for better prognosis for children. We are looking forward to seeing you all and cultivating warm borderless friendships in Tokyo. Your attendance itself, like a growth factor, helps our recover from the disaster. Please join us!!

大澤真木子

Makiko Osawa, MD, PhD Chairperson, Infantile Seizure Society The previous president of Japan Society of Child neurology The president of Japan Epilepsy Society Professor emeritus, Tokyo Women's Medical University

# **ORGANIZATION of ISAE2016**

#### **Organizating Committee**

President: Hideo Yamanouchi Vice-President: Masashi Mizuguchi Secretory General: Yuichi Abe, Mamiko Koshiba

#### **Advisory Board**

Alexis Arzimanoglou (France) Anannit Visudtibhan (Thailand) Ching-Shiang Chi (Taiwan) Federico Vigevano (Italy) Haluk Topaloglu (Turkey) Hian-Tat Ong (Singapore) Jiong Qin (China) Ki Joong Kim (Korea) Kun-Long Hung (Taiwan) Marilyn H Ortiz (Philippines) Phillip L. Pearl (USA) Pratibha Singhi (India) Virginia Wong (China)

#### Program committee

Hideo Yamanouchi (Japan, Chairperson) Akihisa Okumura (Japan) George Imataka (Japan) Hiroshi Sakuma (Japan) Hitoshi Yamamoto (Japan) Junichi Takanashi (Japan) Kei Murayama (Japan) Mitsumasa Fukuda (Japan) Shinichi Hirose (Japan) Shinichi Niijima (Japan) Takanori Yamagata (Japan) Takashi Ichiyama (Japan) Wang-Tso Lee (Taiwan) Yoshihiro Maegaki (Japan)

#### **Bursary Committee**

Hideo Yamanouchi (Chairperson) Masashi Mizuguchi (Japan) Toshisaburo Nagai (Japan) Hideji Hattori (Japan) Shinichi Hirose (Japan) Jun Kohyama (Japan) Hirokazu Oguni (Japan) Yasuhiro Suzuki (Japan)

#### Award Committee

- Platform Presentation Section Mitsuhiro Kato (Chairperson) Akira Oka (Japan) Shinichi Niijima (Japan) Hitoshi Yamamoto (Japan) Hiroshi Sakuma (Japan) Kazuhiro Muramatsu (Japan) Aristea. S. Galanopoulou (USA) Solomon L. Moshé (USA) Phillip L. Pearl (USA) Helen Cross (UK) Raman Sankar (USA) Kai-Ping Chang (Taiwan)
- 2. Poster Presentation Section Toshisaburo Nagai (Chairperson) Shinichi Hirose (Japan) Hirokazu Oguni (Japan) Yasuhiro Suzuki (Japan)

#### **Host Organizer**

Infantile Seizure Society (ISS)

# ACKNOWLEDGEMENT

ISAE2016 has been held under the endorsement from International League against Epilepsy (ILAE), Japan Medical Association (JMA), Asian & Oceanian Child Neurology Association (AOCNA), Japanese Epilepsy Society (JES) and Japanese Society of Child Neurology (JSCN).

The organizing committee of ISAE2016 would like to express sincere thanks to the associations, companies, hospitals and persons to support ISAE2016. The detail financial supports are shown in Page 187.

# **GENERAL INFORMATION**

#### 1. Main topics

Classification of acute encephalopathy, Epidemiology of acute encephalopathy/encephalitis, Pathophysiology of acute encephalopathy/encephalitis, Subtypes of acute encephalopathy in childhood

Autoimmune-mediated encephalitis, Encephalopathy/encephalitis with refractory epileptic status Endemic encephalitis, Management of acute encephalopathy/encephalitis, Sequelae and Managements, and others

#### 2. Target attendees

Pediatricians, neurologists, neurosurgeons, epileptologists, basic and clinical researchers who are interested in epilepsy and patient care in children

#### 3. Official language

English only

#### 4. Visa application

To visit Japan, you must carry a valid passport. A visa is required for citizens of countries which do not have visa-exempt agreements with Japan. Please contact the nearest Japanese Embassy or Consulate for visa application.

Ministry of Foreign Affairs of Japan:

http://www.mofa.go.jp/j\_info/visit/visa/index.html

#### 5. Climate

The weather in Tokyo in early July can be very hot and humid, as it is right in the middle of the rainy season. Consider bring light clothes and a jacket since meeting room temperatures and personal comfort levels vary.

Avarage temparature in July in Tokyo: Average 25.0 °C, Highest 29.2 °C, Lowest 21.8 °C



https://ja.wikipedia.org/wiki/%E9%9B%A8%E6%B8%A9%E5%9B%B3#/media/File:ClimateTokyoJapan.png (Accessed June 10th)

#### 6. Currency exchange

Japanese yen cash or major credit cards are acceptable at regular stores and restaurants.

#### 7. Electricity

Electric current is uniformly 100 volts, AC, throughout Japan.

#### 8. Official Certificate for Attendance and CME Points

An official certificate for attendance at the ISBIS will be prepared for all participants. To Japanese colleagues, authorized CME units will be rewarded by three societies as following CME Points.

Society	Attandanca	Authorship		
Society	Attendance	Presenter	Co-author	
Japan Pediatric Society	3u	Ou	0u	
Japan Epilepsy Society	5u	20u	0u	
Japanese Society of Child Neurology	8u	4u	1u	

max sum up to 12 units u=unit

#### 9. Liabilities

All participants and accompanying persons should be responsible for their own medical, accident and other necessary insurance.

# **REGISTRATION FEE AND CATEGORY**

#### 1. Registration Fee

Category	Early Registration (up to March 31,2016)	Late Registration (From April 1 to May 31, 2016)	Final Registration (From June 1 to July 3, 2016)
Infantile Seizure Society Member AOCNA Member	JPY 23,000-	JPY 26,000-	JPY 28,000-
Non Member	JPY 27,000-	JPY 30,000-	JPY 32,000-
Junior Physician / Resident*** Student	JPY 15,000-	JPY 18,000-	JPY 20,000-
Accompanying Person		FREE	
Grand Social Party		FREE	

(JPY = Japanese YEN)

i. AOCNA\*=Asian & Oceanian Neurology Association

- ii. Junior Physician/Resident\*\*\* =under 30 years of age. Students of post-graduate course are also eligible to this category.Student\*\*: Copy of official documents such as a student's identification or a certificate will be required.
- iii. Copy of official documents such as a student's identification or a certificate will be required. Admission fee for Grand Social Party is FREE (participants need to show the name badge).

#### 2. Entitlements

#### [Participants]

Conference registrants are entitled for the followings:

- 1. Access to all Scientific Sessions, Poster Presentations and Exhibitions
- 2. Opening ceremony, Closing ceremony, Grand social party and Farewell party,
- 3. Coffee breaks and Luncheon seminars
- 4. Congress bag with program and related information and Conference badge

#### [Accompanying Persons]

Registered accompanying persons are entitled for the followings:

- 1. Opening ceremony, Closing ceremony, Grand social party and Farewell party
- 2. Access to Poster Presentations and Exhibition but not to any Scientific Sessions
- 3. Congress Badge

#### 3. On-site Registration

Registration desk will open at

Day 1: Friday, July 1	9:00-18:00
Day 2: Saturday, July 2	9:00-18:00
Day 3. Sunday July 3	9.00-18.00

Please come to the Registration desk, located in front of the entrance of the conference venue to register.

Payment must be made in Japanese Yen only.

#### 4. Social Program

Grand Soc	cial Party
Date:	Saturday, July 2 18:30-20:30
Venue:	Meeting Room, 2nd Floor, NII
	(2-1-2 Hitotsubashi, Chiyoda-ku, Tokyo /Tel: +81-3-3261-1101)
Registr	ration Fee: Free of charge

Farewell Party

Date: Sunday, July 3 17:40-19:30 Venue: Cafeteria, 3rd Floor, NII (2-1-1 Hitotsubashi, Chiyoda-ku, Tokyo /Tel: +81-3-3261-1101) Registration Fee: Free of charge

#### 5. Conference Venue

Hitotsubashi Hall (National Center of Sciences Building/ National Institute of Informatics) 2-1-2 Hitotsubashi, Chiyoda-ku, Tokyo / Tel: +81-3-4212-6000 Access: http://www.nii.ac.jp/en/about/access/

#### 6. Conference Program and Abstracts

Price: 1,000 JPY

# **INSTRUCTIONS FOR ORAL AND POSTER PRESENTATIONS**

#### Instructions for Invited Speakers and Oral Speakers in the Platform Sessions

- 1. A single projection screen without sound is available for presentation.
- 2. Conflict of interest (COI) should be presented ahead of the presentation.
- 3. All speakers are requested to make a registration no later than one hour before the presentation at the PC Data Registration Desk on the 2nd floor.
- 4. We accept slide file attached with your name on, prepared by Microsoft Office PowerPoint 2010 or 2013 using Windows PC, when you bring your slide data saved in USB memory stick or CD-R. To avoid garbled characters, please use standard font which is originally installed by OS. When your presentation includes movies, we strongly recommend to bring your own computer.
- 5. When you bring your own Windows PC or Macintosh computer, make sure that your computer has D-Sub 15 pin mini terminal for monitor output (Figure). Please carry your own connector in case your computer does not have it. Please turn off the screen saver.



- 6. We do not accept video tape presentation.
- 7. All presentations should be done within the allotted time under the management of chairpersons. Speakers in the Platform Sessions 1-6 are requested to adhere strictly to 6 min for presentation and 2 min for discussion (total 8 min). The time-keeper alert you to the remaining and termination time of the presentation.
- 8. The most excellent presentation in the Platform Sessions is commended as Fukuyama Memorial Award at the Closing Ceremony on July 3. Every speaker in the Platform Session is a candidate for the awardee.
- 9. The excellent presentation by young investigator under the age of 40 in the Platform Sessions is commended as Kawano Masanori Special Award at the Closing Ceremony on July 3. This award is sponsored by Kawano Masanori Memorial Public Interest Incorporated Foundation for Promotion of Pediatrics, Japan.

#### Instructions for Discussion

- 1. Active discussions from the floor are encouraged as far as the time is available.
- 2. All aspects of discussion session shall be ordered by due consideration of chairpersons.
- 3. Those who wish to raise a question/discussion may raise their hands and wait to be called by the chairperson. To begin discussion, please identify oneself first.

#### **Next Chairpersons and Next Speakers**

The seats for "Next Speakers" and "Next Chairpersons" are prepared in the front row of the conference room.

Please be seated 15 minutes prior to your presentation/session.

#### Instructions for the Poster Sessions and the Oral Poster Presentations

- 1. The Poster Sessions and the Oral Poster Presentations are held in the Poster Room on the 1st floor.
- 2. All Posters should be set up from 9:00 to 13:00 on July 1, exhibited from 13:00 on July 1 to 15:00 on July 3, and removed from 15:00 to 17:00 on July 3. Posters exhibited after 17:00 on July 3 shall be removed and may be discarded by the staff members of ISAE2016.
- 3. Each speaker is requested to exhibit a top banner within the size of 70 cm in width and 20 cm in height showing the title, names and affiliations on the right side of the poster number sheet set in the left upper corner on the poster board as shown in the figure. The size of the body of poster below the top banner should not exceed 90 cm in width or 160 cm in height. Free pins are provided for poster speakers in the Poster Room. Staple guns are strictly prohibited for mounting.
- 4. The Poster Sessions are scheduled from17:40 to 18:30 on July 1, and from 17:10 to 17:50 on July 2. Each speaker is requested to stay in front of his/her poster for discussion during the Poster Sessions.
- 5. Speakers of the Oral Poster Presentations (OP1-OP10) are requested to make an oral presentation managed by two chairpersons in the Poster Room as follows:
  i. Oral Poster Presentation 1 (OP1-OP5): from 17:00 to 17:40 on July 1



ii. Oral Poster Presentation 2 (OP6-OP10): from 16:30 to 17:10 on July 2iii. Allotted time: 6 minutes for presentation and 2 minutes for discussions.

- 6. Conflict of interest (COI) should be shown in the poster.
- 7. The most excellent poster presentation in the Poster Sessions and the Oral Poster Presentations is commended as Best Poster Award at the Closing Ceremony on July 3. Every speaker in the Poster Sessions and the Oral Poster Presentations is a candidate for the awardee of Best Poster Award.
- 8. Young Investigator Poster Award is provided to an excellent poster presentation by young investigator under the age of 40. The awardee is commended at the Closing Ceremony on July 3.

# VENUE



(http://www.hit-u.ac.jp/hall/file/menu-016/file\_02.pdf, Accessed Aug.10)

#### Hitotsubashi Hall

(National Center of Sciences Building/ National Institute of Informatics)

National Center of Sciences Building 2F, 2-1-2 Hitotsubashi, Chiyoda-ku, Tokyo 101-8439

By train(Subway)

3-5 minutes walk from JIMBOCHO station and TAKEBASHI station

1. "JIMBOCHO" station (3 subway lines available)

Exit A8, A9

Station number:

- Z-07 on Hanzomon Line of Tokyo Metro
- I-10 on Mita Line of Toei Subway
- S-06 on Shinjuku Line of Toei Subway

2. "TAKEBASHI" station

Exit 1b

Station number:

• T-08 on Tozai Line of Tokyo Metro



Inter-University Research Institute Corporation Research Organization of Information and Systems National Institute of Informatics

2-1-2 Hitotsubashi, Chiyoda-ku, Tokyo 101-8430 Tel: +81-3-4212-2000 (Exchange)

By Train (Subway) Tokyo Metro Hanzomon Line / Toei Mita Line / Toei Shinjuku Line "JIMBOCHO" Exit A9 Toyko Metro Tozai Line "TAKEBASHI" Exit 1b 3-5 minutes walk from the stations



Subway Toei Mita Line Yamanote Line

Please refer to the URL below for further details of Access. http://www.nii.ac.jp/en/about/access/

(http://www.nii.ac.jp/en/about/access/, Accessed Aug.10)



# OVERVIEW of DAILY PROGRAM

Time	Day 1, J	luly 1 Fri	Day 2, J	uly 2 Sat	Day 3, July 3 Sun	Time
7:30			ISS Business Meeting (Gakushi Kaikan #203)		7:30-8:50 Book Publishing Meeting (Gakushi Kaikan #203)	7:30
9:00	Registration Start		Registration Start		Registration Start	9:00
10:00	0:00 9:20-12:00 Pre-Congress Educational Program for Leadership Development (Rehearsal Lessons by Experts)		9:30- <b>Diagnosti</b> Jun-ichi 1 Akihisa ( Sooyou	10:30 <b>c Strategy</b> Takanashi Dkumura Ing Lee	9:20-11:00 Encephalopathy/Encephalitis with Refractory Epileptic Status Raman Sankar (Rima Nabbout)	10:00
			ts) 10:30-11:50 Subtypes of Acute Encephalopathy 1 Masashi Shiomi Masashi Mizuguchi I-Jun Chou Hitoshi Osaka		Hiroshi Sakuma Hsiu-Fen Lee Nicola Specchio	
11:00					11:00-11:10 Coffee Break 11:10-12:00 Treatment of Status Epilepticus J. Helen Cross Kuang-Lin Lin	11:00
12:00			12:00	13.00		12:00
			Luncheon Yushiro Y	<b>Seminar 1</b> ′amashita	12:10-13:10 <b>Luncheon Seminar 2</b> J. Helen Cross	
13:00	13:00-13:15 Op	ening Ceremony	13:10	-14:10		13:00
	13:15-13:45 Presidential and Vice Presidental Lectures		13:45 Presidental Lectures 14:30 Subtypes of Acute Encephalopathy 2 Phillip L. Pearl		13:20-14:00 Platform Session 5	
14:00	Keynote	Lecture	Hsiu-F 14:10-14:20	en Lee Coffee Break	14:00 14:50	14:00
	Solomon Moshé				Platform Session 6	
	14.00 14.40	-15:45	14:20 Acute En	-16:20 <b>cephalitis</b>	14:50-15:00 Coffee Break	
15:00	14:40-15:45 <b>Pathophysiology 1</b> Tetsushi Yoshikawa Annamaria Vezzani		Russell Hiroyuk Yukitoshi Pratibha Bin Foo	C. Dale ti Torisu Takahashi a Singhi	15:00-15:50 <b>General Management</b> Sunit Singhi Tatsuya Kawasaki	15:00
16:00	15:45-16:50 <b>Pathophysiology 2</b> Shinichi Hirose		16:20-16:30 Break with	coffee, wine and cheese	15:50-16:30 Therapeutic Hypothermia George Imataka Kuang-I in I in	16:00
	Aristea S. G 16:50-17:00 Break with	alanopoulou	16:30-17:10 Platform Session 3	16:30-17:50 Poster Session	16:30-17:00 Rehabilitation and Home Therapy Hiroshi Arai	
17:00	17:00-17:40 Platform Session 1	17:00-18:30 Poster Session with	17:10-17:50 Platform Session 4	With Wine and Cheese (Oral Poster Presentation 2)	17:00-17:20 Closing Ceremony / Award Ceremony	17:00
18:00	17:40-18:30 Platform Session 2	Wine and Cheese (Oral Poster Presentation 1)			17:40-19:30	18:00
					Farewell Party (Cafeteria 3F)	
19:00	0		18:30 Grand So	-20:30 cial Party		19:00
20:00						20:00

# **Pre-Congress ISAE2016**

# **Educational Program for Leadership Development by Expert**

### Instruction

- 1. Check-in at the registration desk at 9:00.
- 2. Rehearsal Rooms 1-5 are located on the 2nd floor (see FLOOR PLAN for PRE-CONGRESS shown in page 20).
- 3. Your allotted time for presentation is strictly within 6 minutes, followed by educational feedback from executive tutors for 15 minutes.
- 4. A single projection screen without sound is available for your presentation.
- 5. We strongly recommend bringing your slide data saved in USB memory stick or CD-R. When you start your presentation, set up your slide quickly by yourself using Windows PC we prepare.
- 6. When you bring your own Windows PC or Macintosh computer, make sure that your computer has D-Sub 15 pin mini terminal for monitor output. Please carry your own connector in case your computer does not have it.
- 7. Speakers in the oral poster presentation are requested to make a presentation in the same manner as shown above.
- 8. Note that your rehearsal lesson may start earlier than the schedule.
- 9. Student's lunch is not served.

#### Introduction in the Main Hall (9:20-9:25)

Hideo YAMANOUCHI (President ISAE2016) Solomon L. MOSHÉ (Executive Supervisor)

### **Rehearsal Room 1**

Aristea. S. GALANOPOULOU (Executive Tutor) Mitsuhiro KATO (Assistant Tutor)

- 1. G-02 (9:30-9:51)
  - SEIZURES FOLLOWING CHILDHOOD IMMUNIZATION RARE IN BANGLADESH, A COMPREHENSIVE COHORT STUDY Mir ANWAR
- 2. G-04 (9:55-10:16) CEREBROSPINAL FLUID NEOPTERIN AND CYTOKINE ANALYSIS IN PATIENTS WITH ENCEPHALITIS OR ENCEPHALOPATHY Norikatsu HIKITA
- 3. G-05 (10:20-10:41) IDENTIFICATION OF BIOMARKER FOR EARLY DIAGNOSIS OF AESD BY CSF PROTEOMICS ANALYSIS Karin KOJIMA

4. G-07 (10:45-11:06)

HLA VARIANTS AND CYTOKINE GENE POLYMORPHISMS CONFER SUSCEPTIBILITY TO ACUTE NECROTIZING ENCEPHALOPATHY Ai HOSHINO

5. OP-1 (11:10-11:31)

HIGH MOBILITY GROUP BOX 1 ENHANCED ACQUIRED EPILEPSY IN A RODENT MODEL OF INFANTILE FEBRILE STATUS EPILEPTICUS Masanori ITO

6. OP-2 (11:35-11:56) NGS-BASED EPILEPSY GENE PANEL TEST IN EARLY-ONSET CHILDHOOD EPILEPSY Jiwon LEE

#### **Rehearsal Room 2**

Solomon L. MOSHÉ (Executive Supervisor and Executive Tutor) Akira OKA (Assistant Tutor) Kazuhiro MURAMATSU (Assistant Tutor)

1. G-09 (9:30-9:51)

COMPOUND HETEROZYGOUS PIGT MUTATIONS IN AN INFANT WITH SEVERE DEVELOPMENTAL DELAY AND INTRACTABLE MYOCLONIC SEIZURE

Shohei KUSABIRAKI

- 2. G-12 (9:55-10:16) ELECTROENCEPHALOGRAM FINDINGS IN ACUTE EVCEPHALITIS/ ENCEPHALOPATHIES Tatsuya FUKASAWA
- 3. G-13 (10:20-10:41) THE CASE OF CLINICO-ELECTRICAL DISSOCIATION OF ENCEPHALOPATHY Soichiro TODA
- 4. G-14 (10:45-11:06)

TRANSIENTLY REDUCED CORTICAL DIFFUSION IN CHILDREN EXHIBITING PROLONGED FEBRILE SEIZURES Takeshi SUZUKI

5. OP-3 (11:10-11:31)

DRAVET SYNDROME PRESENTING AS WEST SYNDROME SECONDARY TO SCN1A MUTATION- A RARE REPORT OF TWO CASES Vykuntaraju GOWDA

6. OP-4 (11:35-11:56) ELECTROENCEPHALOGRARHY FINDINGS TO PREDICT ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION Atsuko OHNO

#### **Rehearsal Room 3**

Phillip L. PEARL (Executive Tutor) Shinichi NIIJIMA (Assistant Tutor)

1. G-15 (9:30-9:51) LONGITUDINAL BRAIN MRI PATTERN IN JAPANESE ENCEPHALITIS Yukie ARAHATA

- 2. G-18 (9:55-10:16) PROCALCITONIN LEVEL IN ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION Takasu MICHIHIKO
- 3. G-19 (10:20-10:41) **BIOCHEMICAL AND GENETIC PROGNOSTIC FACTORS IN ACUTE** ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION (AESD) Hiroshi MATSUMOTO
- 4. OP-5 (10:45-11:06) TWO CASES OF ACUTE BRAIN SWELLING-TYPE ENCEPHALOPATHY Masataka FUKUOKA
- 5. OP-6 (11:10-11:31) CLINICAL FEATURES AND CEREBROSPINAL FLUID CYTOKINE PROFILE OF PEDIATRIC ANTI-NMDAR ENCEPHALITIS Tomonori SUZUKI

#### **Rehearsal Room 4**

J. Helen CROSS (Executive Tutor) Hitoshi YAMAMOTO (Assistant Tutor)

- 1. G-21 (9:30-9:51) EFFICACY AND CNS DEPRESSION OF SECOND-LINE TREATMENT IN CHILDREN WITH FEBRILE STATUS EPILEPTICUS Masahiro NISHIYAMA
- 2. G-22 (9:55-10:16) COMBINATION OF BUMETANIDE, AN ANTAGONIST OF NKCC1, WITH BENZODIAZEPINES CAN RESCUE THE SEQUELAE OF STATUS EPILEPTICUS OF CHILDHOOD Keisuke NAKAJIMA
- 3. G-24 (10:20-10:41) FACTORS ASSOCIATED WITH INTRACTABLE EPILEPSY AFTER CHILDHOOD ACUTE ENCEPHALOPATHY: A RETROSPECTIVE STUDY OF 74 CASES. Yusuke TAKEZAWA

4. G-25 (10:45-11:06)

WHERE EEG UNRAVELS THE ENCEPHALOPATHY: EPILEPSY WITH CONTINUOUS SPIKES AND WAVES DURING SLOW-WAVE SLEEP IN INDIAN CHILDREN

- Arushi G SAINI
- 5. OP-7 (11:10-11:31) A CASE OF AERRPS WITH PAHLOGICAL FINIDNGS Ayuko YOSHIDA

6. OP-8 (11:35-11:56)

TREATMENT AND PROGNOSIS ASSOCIATED WITH HUMAN PARECHOVIRUS 3 ENCEPHALITIS WITH A NEONATAL ONSET **Kiyohiro KIM** 

#### **Rehearsal Room 5**

Raman SANKAR (Executive Tutor) Shinji SAITOH (Assistant Tutor) Hiroshi SAKUMA (Assistant Tutor)

1. G-28 (9:30-9:51)

AUTOANTIBODY AS A FAVORABLE PROGNOSTIC MARKER !? ~MYELIN-OLIGODENDROCYTE GLYCOPROTEIN ANTIBODIES IN JAPANESE PEDIATRICS WITH ACUTE DISSEMINATED ENCEPHALOMYELITIS~ Naomi HINO-FUKUYO

2. G-29 (9:55-10:16)

THERAPEUTIC RESPONSE TO PULSED INTRAVENOUS METHYL PREDNISOLONE IN PAEDIATRIC ANTI-N-METHYL-D-ASPARTATE-RECEPTOR ENCEPHALITIS (NMDARE) Bindu Parayil SANKARAN

- 3. G-31 (10:20-10:41) CHRONIC ENCEPHALITIS ASSOCIATED WITH ANTI-MYELIN OLIGODENDROCYTE GLYCOPROTEIN ANTIBODIES Hiroya NISHIDA
- 4. OP-9 (10:45-11:06) PROGNOSTIC OVERVIEW OF EPILEPTIC ENCEPHALOPATHIES STARTING IN THE INFANTILE PERIOD Kanako TAKEDA
- 5. OP-10 (11:10-11:31) ABERRANT IMMUNE ACTIVATION IN THE CENTRAL NERVOUS SYSTEM OF FEBRILE INFECTION-RELATED EPILEPSY SYNDROME (FIRES) Ayuko IGARASHI



# PROGRAM

The 18th Annual Meeting of Infantile Seizure Society

# International Symposium on Acute Encephalopathy in Infancy and Its Related Disorders (ISAE2016)

# PROGRAM

# DAY1, FRIDAY, JULY 1

- 9:00-18:00 Registration
- 9:20-12:00 **Pre-congress: Educational Program for Leadership Development**
- 13:00-13:15 **Opening Ceremony**

#### **Presidential Lecture**

13:15-13:25 L-01 OVERVIEW OF ISAE2016 Hideo YAMANOUCHI Department of Pediatrics, Saitama Medical University, Saitama, Japan

#### Vice-presidential Lecture Chairperson: Hideo Yamanouchi (Japan)

13:25-13:45 L-02 DEFINITION, CLASSIFICATION AND EPIDEMIOLOGY OF ACUTE ENCEPHALOPATHY Masashi MIZUGUCHI Department of Developmental Medical Sciences, The University of Tokyo, Tokyo, Japan

#### Keynote Lecture (sponsored by Eisai) Chairperson: Makiko Osawa (Japan)

13:45-14:30 L-03
 INSIGHTS INTO SEIZURES AND EPILEPSIES IN THE DEVELOPING BRAIN: TRANSLATIONAL STUDIES
 Solomon L. MOSHÉ
 Saul R. Korey Department of Neurology, Dominick P. Purpura Department Neuroscience and Department of Pediatrics, Albert Einstein College of Medicine and

Montefiore Medical Center, Bronx, New York, USA

#### Pathophysiology 1 Chairpersons: Mitsumasa Fukuda (Japan), Federico Vigevano (Italy)

#### 14:40-15:10 **L-04**

#### NEUROVIRULENCE OF HUMAN HERPESVIRUS 6B (HHV-6B): ENCEPHALITIS AND MESIAL TEMPORAL LOBE EPILEPSY Tetsushi YOSHIKAWA

Department of Pediatrics, Fujita Health University, Toyoake, Japan

#### 15:10-15:45 **L-05**

#### ICTOGENIC AND EPILEPTOGENIC MECHANISMS OF NEUROINFLAMMATION: INSIGHTS FROM ANIMAL MODELS Annamaria VEZZANI

Department of Neuroscience, IRCCS-Istituto di Ricerche Farmacologiche Mario Negri, Milano, Italy

## Pathophysiology 2

Chairpersons: Mitsuhiro Kato (Japan), Ki Joong Kim (Korea)

15:45-16:15 **L-06** 

### **GENETIC BACKGROUND OF ENCEPHALOPATHY** Shinichi HIROSE

Department of Pediatrics, School of Medicine, Fukuoka University, Fukuoka, Japan

#### 16:15-16:50 **L-07**

## NEUROINFLAMMATION IN THE PATHOGENESIS OF EARLY LIFE EPILEPTIC ENCEPHALOPATHIES

#### Aristea S. GALANOPOULOU

Saul R. Korey Department of Neurology, Albert Einstein College of Medicine, Bronx, NY, USA

#### 16:50-17:00 Break with coffee, wine and cheese

#### Platform Session 1: Pathophysiology

Chairpersons: Takanori Yamagata (Japan), Asuri Prasad (Canada)

17:00-17:40 **G-01** 

### EFFECT OF OCIMUM BASILICUM HYDROALCOHOLIC EXTRACT AGAINST PENTYLENTETRAZOLE-INDUCED SEIZORE IN ANIMAL MODEL

#### Mehrdad MODARESI

Biology Faculty, Isfahan (Khorasgan) Branch, Islamic Azad University, Isfahan, Iran

#### G-02

SEIZURES FOLLOWING CHILDHOOD IMMUNIZATION RARE IN BANGLADESH, A COMPREHENSIVE COHORT STUDY Mir ANWAR

Department of Health, South Africa

#### G-03

#### FEVER ACTIVATES MICROGLIA TO ENGULF INHIBITORY SYNAPSES AND LOWER THE SEIZURE THRESHOLD Ryuta KOYAMA

Laboratory of Chemical Pharmacology, Graduate School of Pharmaceutical Sciences, The University of Tokyo, Tokyo, Japan

#### G-04

## CEREBROSPINAL FLUID NEOPTERIN AND CYTOKINE ANALYSIS IN PATIENTS WITH ENCEPHALITIS OR ENCEPHALOPATHY

#### Norikatsu HIKITA

Department of Pediatrics, Graduate School of Medicine, Osaka City University, Osaka, Japan

#### G-05

# IDENTIFICATION OF BIOMARKER FOR EARLY DIAGNOSIS OF AESD BY CSF PROTEOMICS ANALYSIS

#### Karin KOJIMA

Department of Pediatrics, Jichi Medical University, Shimotsukeshi Tochigi, Japan

### **Platform Session 2: Genetics**

Chairpersons: Jun Tohyama (Japan), Phillip L. Pearl (USA)

#### 17:40-18:30 **G-06**

# GENETIC PRDISPOSITION TO ACUTE ENCEPHALOPATHY WITH STATUS EPILEPTICUS

#### Makiko SAITOH

Department of Developmental Medical Sciences, The University of Tokyo, Tokyo, Japan

#### G-07

## HLA VARIANTS AND CYTOKINE GENE POLYMORPHISMS CONFER SUSCEPTIBILITY TO ACUTE NECROTIZING ENCEPHALOPATHY

#### Ai HOSHINO

Department of Developmental Medical Sciences, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

Department of Pediatrics, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

#### G-08

#### EARLY ONSET EPILEPTIC ENCEPHALOPATHY -AN UNUSUAL PHENOTYPE WITH MULTISYSTEM INVOLVEMENT RELATED TO A PATHOGENIC SCN1A MUTATION

#### Asuri N PRASAD

Department of Pediatrics & Division of Clinical Neurosciences, Western University and London Health Sciences Centre, London, Ontario, Canada

#### G-09

#### COMPOUND HETEROZYGOUS PIGT MUTATIONS IN AN INFANT WITH SEVERE DEVELOPMENTAL DELAY AND INTRACTABLE MYOCLONIC SEIZURE

#### Shohei KUSABIRAKI

Department of Child Neurology, National Center Hospital, National Center of Neurology and Psychiatry, Tokyo, Japan

#### G-10

## A NOVEL KCNQ2 MUTATION IN FAMILIAL EARLY-ONSET EPILEPTIC ENCEPHALOPATHY

#### Yuan-feng ZHOU

Department of Neurology, Children's Hospital of Fudan University, Shanghai, China

#### G-11

## A CASE OF FAMILIAL ACUTE NECROTIZING ENCEPHALOPATHY WITH NOVEL GENE MUTATION FROM INDIA

#### **Prashant Ramesh UTAGE**

Department of Pediatrics, Lotus Hospital For Women and Children, Hyderabad, India Department of Early Intervention, Utage Child Neuro Clinic and Development Centre, Hyderabad, India

Oral Poster Presentation 1 (The Poster Room on the 1st floor) Chairpersons: Shinji Saitoh (Japan), Nicola Specchio (Italy)

#### 17:00-17:40 **OP-01**

### HIGH MOBILITY GROUP BOX 1 ENHANCED ACQUIRED EPILEPSY IN A RODENT MODEL OF INFANTILE FEBRILE STATUS EPILEPTICUS

#### **Masanori ITO**

Department of Pediatrics, Ehime University Graduate School of Medicine, Toon, Ehime, Japan

# OP-02

## NGS-BASED EPILEPSY GENE PANEL TEST IN EARLY-ONSET CHILDHOOD EPILEPSY

#### **Jiwon LEE**

Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

#### OP-03

#### DRAVET SYNDROME PRESENTING AS WEST SYNDROME SECONDARY TO SCN1A MUTATION- A RARE REPORT OF TWO CASES

#### Vykuntaraju GOWDA

Indira Gandhi Institute of Child Health, Bangalore, India

#### OP-04

#### ELECTROENCEPHALOGRARHY FINDINGS TO PREDICT ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION

#### Atsuko OHNO

Department of Pediatrics, Nagoya University, Nagoya, Japan

#### OP-05

# TWO CASES OF ACUTE BRAIN SWELLING-TYPE ENCEPHALOPATHY

#### Masataka FUKUOKA

Department of Pediatric Emergency, Osaka General City Hospital, Osaka, Japan

#### Poster Session (The Poster Room on the 1st floor)

17:40-18:30 **P-01~P-35** 

19:00-20:30 Welcome Reception (Invitees Only)

# DAY2, SATURDAY, JULY 2

#### 9:00-18:00 Registration

#### Diagnostic Strategy

Chairpersons: Shinichi Niijima (Japan), Raman Sankar (USA)

9:30-9:50 **L-08** 

### NEUROIMAGING IN ACUTE ENCEPHALOPATHY IN JAPAN Jun-ichi TAKANASHI

Department of Pediatrics, Yachiyo Medical Center, Yachiyo, Japan

- 9:50-10:10 L-09 ELECTROENCEPHALOGRAPHY IN CHILDREN WITH ACUTE ENCEPHALOPATHY Akihisa OKUMURA Department of Pediatrics, Aichi Medical University, Nagakute, Japan
- 10:10-10:30 L-10 EEG FINDINGS DURING ACUTE PHASE OF PROLONGED FEBRILE SEIZURES AND PEDIATRIC ACUTE ENCEPHALOPATHY

#### Sooyoung LEE

Department of Critical Care Medicine, Fukuoka Children's Hospital, Fukuoka , Japan

#### Subtypes of Acute Encephalopathy 1 Chairpersons: Yasuhiro Suzuki (Japan), Kuang-Lin Lin (Taiwan)

10:30-10:50 **L-11** 

#### ACUTE ENCEPHALOPATHY WITH FEBRILE CONVULSIVE STATUS(AEFCSE/AESD) and HHE SYNDROME : ACUTE BRAIN DAMAGE PROVOKED BY FEBRILE STATUS EPILEPTICUS Masashi SHIOMI

Department of Pediatrics, Aizenbashi Hospital, Osaka, Japan Department of Pediatric Emergency Medicine(before 2011), Osaka, Japan

10:50-11:10 L-12

# ACUTE NECROTIZING ENCEPHALOPATHY: CLINICAL, PATHOLOGIC AND GENETIC STUDIES

#### Masashi MIZUGUCHI

Department of Developmental Medical Sciences, The University of Tokyo, Tokyo, Japan

#### Subtypes of Acute Encephalopathy 1 Chairpersons: Akira Ohtake (Japan) , Wang-Tso Lee (Taiwan)

11:10-11:30 **L-13** 

#### ACUTE NECROTIZING ENCEPHALOPATHY IN TAIWAN AND GLOBAL STUDY ON ACUTE ENCEPHALOPATHY I-Jun CHOU

Department of Pediatrics, Division of Pediatric Neurology, Chang Gung Children's Hospital and Chang Gung University, Kwei-Shan, Tao Yuan, Taiwan

#### 11:30-11:50 **L-14**

#### ACUTE ENCEPHALOPATHY AS AN INITIAL MANIFESTATION OF MITOCHONDRIAL DIEASES AND RELATED DISORDERS Hitoshi OSAKA

Department of Pediatrics, Jichi Medical University, Shimotsuke, Japan

Luncheon Seminar 1 (The Conference Room adjacent to the Main Hall, sponsored by Eli Lilly Japan) Chairperson: Eiji Nakagawa (Japan)

#### 12:00-13:00 **L-15**

#### ENCEPHALITIS/ENCEPHALOPATHY AND NEURODEVELOPMENTAL DISORDERS Yushiro YAMASHITA

Department of Pediatrics & Child Health, Kurume University School of Medicine, Kurume, Japan

Subtypes of Acute Encephalopathy 2 Chairpersons: Akira Oka (Japan), Ching-Shiang Chi (Taiwan)

#### 13:10-13:50 **L-16**

### GENETIC-METABOLIC DISORDERS PRESENTING AS ACUTE, BUT REVERSIBLE, SEVERE EPILEPSIES

#### Phillip L. PEARL

Department of Neurology, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA

#### 13:50-14:10 **L-17**

#### ACUTE ENCEPHALOPATHY IN INFANTS WITH SULFITE OXIDASE AND MOLYBDENUM COFACTOR DEFICIENCY Hsiu-Fen LEE

Department of Pediatrics, Taichung Veterans General Hospital, Taichung, Taiwan

#### 14:10-14:20 Coffee Break

#### Acute Encephalitis 1

Chairpersons: Kazuhiro Muramatsu (Japan), Aristea S. Galanopoulou (USA)

14:20-15:00 **L-18** 

#### OVERVIEW OF CLINICAL RECOGNITION, AUTOANTIBODY DIAGNOSTIC MARKERS AND TREATMENT OF AUTOIMMUNE ENCEPHALITIS

#### **Russell C. DALE**

Institute for Neuroscience and Muscle Research, the Children's Hospital at Westmead, University of Sydney, Australia

#### Acute Encephalitis 2 Chairpersons: Masakazu Mimaki (Japan), Russell Dale (Australia)

15:00-15:20 L-19

# NATIONWIDE SURVEY OF ACUTE DESSEMINATED ENCEPHALOMYELITIS IN JAPAN

#### Hiroyuki TORISU

Department of Pediatrics, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

#### 15:20-15:40 **L-20**

## EARLY CLINICAL DIAGNOSIS & EVIDENCE FOR TREATMENT IN IMMUNE-MEDIATED ENCEPHALITIS WITH ANTIBODIES TO NMDA-TYPE GLURS

#### Yukitoshi TAKAHASHI

National Epilepsy Center, Shizuoka Institute of Epilepsy and Neurological Disorder, NHO, 886 Urushiyama, Aoi-ward, Shizuoka, Japan

#### Acute Encephalitis 3 Chairpersons: Tetsushi Yoshikawa (Japan), Meltem Uzun (Turkey)

#### 15:40-16:10 L-21 ENCEPHALITIS IN THE TROPICS Pratibha SINGHI Department of Pediatrics Advanced Pediat

Department of Pediatrics, Advanced Pediatrics Centre, Postgraduate Institute of Medical Education & Research, Chandigarh. India

16:10-16:20 L-22

## CLUSTERING OF ACUTE FLACCID MYELITIS OF UNKNOWN ETIOLOGY IN JAPAN, AUTUMN 2015

#### Pin Fee CHONG

Department of Pediatric Neurology, Fukuoka Children's Hospital, Fukuoka, Japan

#### 16:20-16:30 Break with coffee, wine and cheese

#### Platform Session 3: Diagnostic strategy/Subtypes of acute encephalopathy Chairpersons: Kenji Sugai (Japan), Kai-Ping Chang (Taiwan)

#### 16:30-17:10 **G-12**

### ELECTROENCEPHALOGRAM FINDINGS IN ACUTE EVCEPHALITIS / ENCEPHALOPATHIES

#### Tatsuya FUKASAWA

Department of Pediatrics, Anjo Kosei Hospital, Anjo, Japan

#### G-13

# THE CASE OF CLINICO-ELECTRICAL DISSOCIATION OF ENCEPHALOPATHY

#### Soichiro TODA

Department of Pediatrics, Kameda Medical Center, Chiba, Japan

#### G-14

TRANSIENTLY REDUCED CORTICAL DIFFUSION IN CHILDREN EXHIBITING PROLONGED FEBRILE SEIZURES

#### Takeshi SUZUKI

Department of Pediatrics, Anjo Kosei Hospital, Anjo, Japan

#### G-15

# LONGITUDINAL BRAIN MRI PATTERN IN JAPANESE ENCEPHALITIS

### Yukie ARAHATA

Department of Pediatrics, Asahi General Hospital, Chiba, Japan

G-16

#### CLINICAL PHENOTYPES AND GENETIC FINDINGS IN CHILDREN WITH MITOCHONDRIAL ENCEPHALOPATHIES: STUDY FROM A TERTIARY CARE UNIVERSITY HOSPITAL IN SOUTH INDIA Bindu Bonovil SANKADAN

#### **Bindu Parayil SANKARAN**

Department of Neurology, National Institute of Mental Health And Neurosciences, Bangalore, India

#### Platform Session 4: Subtypes of acute encephalopathy

Chairpersons: Masayuki Sasaki (Japan), Marilyn Hebron Ortiz (Philippines)

#### 17:10-17:50 **G-17**

### BRAIN MRI AND ITS CONSECUTIVE EPILEPTIC SEIZURES IN A BOY WITH ORNITHINE TRANSCARBAMYLASE DEFICIENCY AND PATERNAL LIVER TRANSPLANTATION

#### **Tatsuro IZUMI**

Department of Pediatrics and Child Neurology, National Nanao Hospital, Nanao, Japan

#### G-18

# PROCALCITONIN LEVEL IN ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION

#### Michihiko TAKASU

Department of Pediatrics, Aichi Medical University Graduate School of Medicine, Aichi, Japan

#### G-19

#### BIOCHEMICAL AND GENETIC PROGNOSTIC FACTORS IN ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION (AESD)

#### Hiroshi MATSUMOTO

Department of Pediatrics, National Defense Medical College, Tokorozawa, Japan

#### G-20

#### ACUTE NECROTIZING ENCEPHALOPATHY OF CHILDHOOD AND ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION- A DEVELOPING COUNTRY EXPERIENCE

#### Arushi Gahlot SAINI

Pediatric Neurology and Neurodevelopmental Unit, Department of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh-160012, India

#### Oral Poster Presentation 2 (The Poster Room on the 1st floor) Chairpersons: Anannit Visudtibhan (Thailand), Pratibha D. Singhi (India)

#### 16:30-17:10 **OP-06**

#### CLINICAL FEATURES AND CEREBROSPINAL FLUID CYTOKINE PROFILE OF PEDIATRIC ANTI-NMDAR ENCEPHALITIS Tomonori SUZUKI

#### Developmental Neuroimmunology Project, Department of Brain Development and Neural Regeneration, Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan

## OP-07

#### A CASE OF AERRPS WITH PATHOLOGICAL FINIDNGS Ayuko YOSHIDA

Department of Pediatrics, Matsuyama Red Cross Hospital, Ehime, Japan

#### OP-08 TREATMENT AND PROGNOSIS ASSOCIATED WITH HUMAN PARECHOVIRUS 3 ENCEPHALITIS WITH A NEONATAL ONSET Kiyohiro KIM

Department of Pediatric Neurology, Osaka City General Hospital, Osaka, Japan

#### **OP-09**

# PROGNOSTIC OVERVIEW OF EPILEPTIC ENCEPHALOPATHIES STARTING IN THE INFANTILE PERIOD

#### Kanako TAKEDA

Department of Pediatrics, St. Marianna University School of Medicine, Kawasaki, Japan

#### **OP-10**

## ABERRANT IMMUNE ACTIVATION IN THE CENTRAL NERVOUS SYSTEM OF FEBRILE INFECTION-RELATED EPILEPSY SYNDROME (FIRES)

#### Ayuko IGARASHI

Department of Pediatrics, Juntendo University Faculty of Medicine, Tokyo, Japan

#### Poster Session (The Poster Room on the 1st floor)

17:10-17:50 **P-01~P-35** 

18:30-20:30 Grand Social Party (The Conference Room adjacent to the Main Hall)

# DAY3, SUNDAY, JULY 3

#### 9:00-18:00 Registration

Encephalopathy/Encephalitis with Refractory Epileptic Status 1 Chairpersons: Jun Natsume (Japan), Haluk Topaloglu (Turkey)

#### 9:20-10:00 L-23

# ACUTE ENCEPHALOPATHY WITH INFLAMMATION-MEDIATED STATUS EPILEPTICUS

#### **Raman SANKAR**

Department of Neurology and Pediatrics, David Geffen School of Medicine, the University of California (Rima Nabbout) (Department of Pediatric Neurology, Paris Descartes University, France)

#### 10:00-10:20 L-24

#### LIGHT FIRES IN THE BRAIN: DOES NEUROINFLAMMATION TRIGGER REFRACTORY STATUS EPILEPTICUS? Hiroshi SAKUMA

Developmental Neuroimmunology Project, Department of Brain Development and Neural Regeneration, Tokyo Metropolitan Institute of Medical Science Tokyo, Japan

#### Encephalopathy/Encephalitis with Refractory Epileptic Status 2 Chairpersons: Hitoshi Yamamoto (Japan), Hian-Tat Ong (Singapore)

10:20-10:40 L-25

## FEBRILE INFECTION-RELATED EPILEPSY SYNDROME (FIRES): LONG-TERM NEUROLOGICAL FOLLOW-UP

#### Hsiu-Fen LEE

Department of Pediatrics, Taichung Veterans General Hospital, Taichung, Taiwan

#### 10:40-11:00 L-26

#### FEBRILE INFECTION RELATED SYNDROME (FIRES): CLINICAL EXPERIENCE IN ITALY Nicola SPECCHIO

Department of Neuroscience, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy

11:00-11:10 Coffee Break

#### Treatment of Status Epilepticus Chairpersons: Takao Takahashi (Japan) , Kun-Long Hung (Taiwan)

11:10-11:40 **L-27** 

#### CURRENT MANAGEMENT OPTIONS IN STATUS EPILEPTICUS J. Helen CROSS

UCL-Institute of Child Health, Great Ormond Street Hospital for Children, London, UK

#### 11:40-12:00 L-28 MULTIMODAL APPROACH, MONITORING AND MANAGEMENT FOR FEBRILE REFRACTORY STATUS EPILEPTICUS Kuang-Lin LIN

Division of Pediatric Neurology, Chang Gung Children's Hospital and Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Taoyuan, Taiwan Luncheon Seminar 2 (The Conference Room adjacent to the Main Hall, sponsored by UCB Japan) Chairperson: Solomon L. Moshé (USA)

12:10-13:10 L-29

#### THE DRUGS DON'T WORK – WHAT NEXT?

#### J. Helen CROSS

UCL-Institute of Child Health, Great Ormond Street Hospital for Children, London, UK

Platform Session 5: Management of status epilepticus and intractable epilepsy Chairpersons: Hirokazu Oguni (Japan), Virginia Wong (China)

#### 13:20-14:00 G-21

#### EFFICACY AND CNS DEPRESSION OF SECOND-LINE TREATMENT IN CHILDREN WITH FEBRILE STATUS EPILEPTICUS

#### **Masahiro NISHIYAMA**

Department of Pediatrics, Kobe University Graduate School of Medicine, Kobe, Japan Department of Neurology, Hyogo Prefectural Kobe Children's Hospital, Kobe, Japan

#### G-22

#### COMBINATION OF BUMETANIDE, AN ANTAGONIST OF NKCC1, WITH BENZODIAZEPINES CAN RESCUE THE SEQUELAE OF STATUS EPILEPTICUS OF CHILDHOOD

#### Keisuke NAKAJIMA

Department of brain development and neural regeneration, Neural development project, Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan

#### G-23

# SEIZURE REMISSION ON PERAMPANEL IN SIALIDOSIS WITH PROGRESSIVE MYOCLONIC EPILEPSY

#### **Kun-Long HUNG**

Department of Pediatrics, Cathay-General Hospital, Taipei, Taiwan School of Medicine, Fu-Jen Catholic University, New Taipei, Taiwan

#### G-24

#### FACTORS ASSOCIATED WITH INTRACTABLE EPILEPSY AFTER CHILDHOOD ACUTE ENCEPHALOPATHY: A RETROSPECTIVE STUDY OF 74 CASES

#### Yusuke TAKEZAWA

Department of Pediatric Neurology, Takuto rehabilitation center for children, Miyagi Children's Hospital, Sendai, Japan

#### G-25

#### WHERE EEG UNRAVELS THE ENCEPHALOPATHY: EPILEPSY WITH CONTINUOUS SPIKES AND WAVES DURING SLOW-WAVE SLEEP IN INDIAN CHILDREN

#### Arushi Gahlot SAINI

Pediatric Neurology and Neurodevelopmental Unit, Department of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh-160012, India Platform Session 6: Autoimmune-mediated Encephalitis/ AREEPS/FIRES Chairpersons: Takashi Ichiyama (Japan), Masanori Takeoka (USA)

#### 14:00-14:50 **G-26**

#### FEBRILE INFECTION- RELATED EPILEPSY SYNDROME (FIRES): A CASE REPORT

#### **Allyn Nicole LIM**

Philippine General Hospital, Manila, Philippines

#### G-27

### TWO CASES OF ACUTE ENCEPHALITIS WITH REFRACTORY, REPETITIVE PARTIAL SEIZURES TREATED WITH LEVETIRACETAM

#### Kaori MIZUKAWA

Department of Pediatrics, Gifu Prefectural General Medical Center, Gifu, Japan Department of Pediatrics, Ichinomiyanishi Hospital, Ichinomiya, Japan

#### G-28

#### AUTOANTIBODY AS A FAVORABLE PROGNOSTIC MARKER ~MYELIN-OLIGODENDROCYTE GLYCOPROTEIN ANTIBODIES IN JAPANESE PEDIATRICS WITH ACUTE DISSEMINATED ENCEPHALOMYELITIS~

#### Naomi HINO-FUKUYO

Center of Genomic Medicine, Tohoku University Hospital, Sendai, Japan Department of Pediatrics, Tohoku University School of Medicine, Sendai, Japan

#### G-29

#### THERAPEUTIC RESPONSE TO PULSED INTRAVENOUS METHYL PREDNISOLONE IN PAEDIATRIC ANTI-N-METHYL-D-ASPARTATERECEPTOR ENCEPHALITIS (NMDARE) Bindu Banavil SANKADAN

#### **Bindu Parayil SANKARAN**

Depts of Neurology, National Institute of Mental Health And Neurosciences, Bangalore, India

#### G-30

#### ANTI-HU ANTIBODY ASSOCIATED NEUROLOGICAL DISEASE, PRESENTING WITH HEMISPHERIC ENCEPHALOPATHY AND INTRACTABLE EPILEPSY IN CHILDREN

#### Masanori TAKEOKA

Division of Epilepsy and Clinical Neurophysiology, Department of Neurology, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts, USA

#### G-31

# CHRONIC ENCEPHALITIS ASSOCIATED WITH ANTI-MYELIN OLIGODENDROCYTE GLYCOPROTEIN ANTIBODIES

## Hiroya NISHIDA

Department of Neuropediatrics, Tokyo Metropolitan Neurological Hospital, Tokyo, Japan

14:50-15:00 Coffee Break

#### General Management Chairpersons: Ikuya Ueta (Japan), Sunit Singhi (India)

#### 15:00-15:30 **L-30**

# INTENSIVE CARE MANAGEMENT OF ACUTE ENCEPHALOPATHY AND ACUTE ENCEPHALITIS

#### Sunit SINGHI

Department of Pediatrics, MM Institute of Medical Sciences and Research, MM University, Mullana-Ambala, India

#### 15:30-15:50 **L-31**

## GENERAL MANAGEMENT OF ACUTE VIRAL ENCEPHALITIS/ ENCEPHALOPATHY IN JAPAN

#### Tatsuya KAWASAKI

Department of Pediatric Critical Care, Shizuoka Children's Hospital, Shizuoka, Japan

#### Therapeutic Hypothermia Chairpersons: Hirokazu Sakai (Japan), Raman Sankar (USA)

15:50-16:10 L-32

# THERAPEUTIC BRAIN MILD HYPOTHERMIA FOR CHILDHOOD ACUTE ENCEPHALOPATHY

#### George IMATAKA

Department of Pediatrics, Dokkyo Medical University, Tochigi, Japan

#### 16:10-16:30 **L-33**

# THE ROLE OF THERAPEUTIC HYPOTHERMIA FOR EPILEPSY AND AUTOIMMUNE ENCEPHALITIS

#### Kuang-Lin LIN

Division of Pediatric Neurology, Chang Gung Children's Hospital and Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Taoyuan, Taiwan

#### Rehabilitation and Management of Home Therapy Chairpersons: Kazuhiro Haginoya (Japan) , Nicola Specchio (Italy)

16:30-17:00 L-34 REHABILITATION AND COMPREHENSIVE INTERVENTION FOR ACUTE ENCEPHALITIS/ENCEPHALOPATHY IN CHILDHOOD Hiroshi ARAI Department of Pediatrics, Morinomiya Hospital, Osaka, Japan

#### 17:00-17:20 Award Ceremony & Closing Ceremony

#### 17:40-19:30 **Farewell Party (the Cafeteria on the 3rd floor)**
## P-01

# RESTING-STATE NETWORKS IN AN INFANT WITH EARLY ONSET EPILEPTIC ENCEPHALOPATHY WITH BUSRT-SUPPRESSION PATTERN ON EEG

Hiroyuki KIDOKORO Department of Pediatrics, Nagoya University Graduate School of Medicine, Nagoya, Japan

#### P-02

#### GOREISAN SUPPRESSES CEREBRAL EDEMA ASSOCIATED WITH HYPOXIC-ISCHEMIC ENCEPHALOPATHY IN CHILDHOOD RATS VIA THE INHIBITION OF AQUAPORIN 4

Yoshiaki YANO Department of Pediatrics, National Hospital Organization Ehime Medical Center, Toon, Ehime, Japan

#### P-03

# POTENTIAL EFFECTS OF ANTIEPILEPTIC DRUGS ON GROWTH VELOCITY IN EPILEPTIC CHILDREN- EXPERIENCE IN ONE MEDICAL CENTER

Shyi-Jou CHEN Department of Pediatrics, Tri-Service General Hospital, National Defense Medical Center, Taichung, Taiwan

### P-04

#### TWO NOVEL SCN1A MUTATIONS IN TURKISH CHILDREN WITH DRAVET SYNDROME

Mutluay ARSLAN Department of Pediatric Neurology, Gülhane Military Medical School, Ankara, Turkey

### P-05

#### ACUTE ENCEPHALOPATHY ASSOCIATED WITH CHRONOLOGICAL EEG CHANGES AND A FATAL CLINICAL COURSE: A CASE STUDY

Tetsuo KUBOTA Department of Pediatrics, Anjo Kosei Hospital, Anjo, Japan

### P-06

# THE CHANGE OF ELECTROENCEPHALOGRAM CAN BE A POTENTIAL PREDICTOR FOR NEONATAL SEIZURES

Wang-Tso LEE Department of Pediatrics, National Taiwan University Children's Hospital, Taipei, Taiwan

### **P-07**

#### SERUM N-TERMINAL PRO-B-TYPE NATRIURETIC PEPTIDE LEVELS ARE ELAVATED DURING ACUTE ENCEPHALOPATHY

Miho FUKUI Department of Pediatrics, Osaka Medical College, Osaka, Japan

### P-08

#### SEIZURE CHARACTERISTICS OF EPILEPSY IN CHILDHOOD AFTER ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION

Yuji ITO Department of Pediatrics, Nagoya University Graduate School of Medicine, Aichi, Japan

P-09

#### DISRUPTED GLUTAMATE-GLUTAMINE CYCLE IN ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION(AESD)

**Eri OGUNI** Department of Pediatrics, Tokyo Women's Medical University, Yachiyo Medical Center, Yachiyo, Japan,

## P-10

# PAROXYSMAL SYMPATHETIC HYPERACTIVITY DURING THERAPEUTIC HYPOTHERIMIA IN A CASE WITH SEVERE AESD

Yuko ICHIMIYA Department of Pediatrics, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan / Emergency and Critical Care Center, Kyushu University, Fukuoka, Japan

## P-11

#### INTRAVENOUS IMMUNOGLOBULIN TREATMENT FOR PETITENS WITH POSTENCEPHALOPATHIC EPILEPSY AFTER ACUTE ENCEPHELOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION

**Kenji INOUE** Department of Pediatrics, Shiga Medical Center for Children, Shiga, Japan

### P-12

#### DISTINGUISHING ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUSED DIFFUSION FROM PROLONGED FEBRILE SEIZURES BY ACUTE PHASE EEG SPECTRUM ANALYSIS

Masayoshi OGURI Division of Child Neurology, Department of Brain and Neurosciences, Faculty of Medicine, Tottori University, Yonago, Japan

### P-13

#### SEQUENTIAL GLASGOW COMA SCALE EVALUATION IS THE MOST WORTHWHILE WAY FOR EARLY DETECTION OF ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION

Tetsuhiro FUKUYAMA Division of Neurology, Nagano Children's Hospital, Azumino, Japan

## P-14

# DEXTROMETHORPHAN AND CYCLOSPORINE A FOR ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION

Toshiyuki MAEDA Department of Pediatrics, Faculty of Medicine, Saga University, Saga, Japan

#### P-15

#### A CASE OF DRAVET SYNDROME AFFECTED AN ACUTE ENCEPHALOPATHY

Tatsuyuki SOKODA Department of Pediatrics, Shiga University of Medical Science, Shiga, Japan

### P-16

#### CASE SERIES OF FATAL ACUTE ENCEPHALOPATHY

Kazumi TOMIOKA Department of Pediatrics, Kobe University Graduate School of Medicine, Kobe, Japan

### P-17

# A CASE REPORT WITH LATE-ONSET MAPLE SYRUP URINE DISEASE PRESENTED AS EPILEPTIC ENCEPHALOPATHY

Meltem UZUN Dortcelik Children Hospital, Turkey

### P-18

#### A CASE OF SEVERE HYPOGLYCEMIC ENCEPHALOPATHY CAUSED BY HYPOCARNITINEMIA DUE TO CEFTERAM PIVOXIL

Kaori SASSA Department of Pediatrics, Saitama Medical University, Japan



#### SIBLINGS WITH LIMBIC ENCEPHALITIS

Sho NARAHARA Department of Pediatric Neurology, Aichi Children's Health and Medical Center, Obu, Japan

## P-20

ACUTE DISSEMINATED ENCEPHALOMYELITIS: CLINICAL PROFILE, MAGNETIC RESONANCE IMAGING FINDINGS AND OUTCOME IN A COHORT OF 35 CHILDREN

Bindu Parayil SANKARAN Dept of Neurology, National Institute of Mental Health & Neurosciences, Bangalore, India

## P-21

A COMPARATIVE STUDY OF TWO CHILD CASES OF ANTI-NMDA RECEPTOR ENCEPHALITIS IN OUR HOSPITAL

Sotaro YUZAWA Department of pediatrics, Gifu prefectual general medical center, Japan

### P-22

DIFFERENCE OF RESPONSE TO KETOGENIC DIET IN 2 CHILDREN WITH ACUTE ENCEPHALITIS WITH REFRACTORY, REPETITIVE PARTIAL SEIZURES

Yu OKAI Department of Pediatrics, Nagoya University, Nagoya, Japan

### P-23

# ACUTE ENCEPHALITIS WITH REFRACTORY, REPETITIVE PARTIAL SEIZURES (AERRPS); A CLINICAL STUDY OF FIVE CHRONIC CASES

Noriko SAWAURA Department of Padiatrics, Gunma University, Graduate School of Medicine, Gunma, Japan

P-24

PATHOGENIC AGENTS DETECTED AMONG ACUTE ENCEPHALITIS AND ENCEPHALOPATHY CASES LESS THAN 5 YEARS OF AGE, JAPAN, 2011-2015

**Hideo OKUNO** Infectious Disease Surveillance Center, National Institute of Infectious Diseases, Tokyo, Japan

## P-25

# A CASE OF SCRUB TYPHUS MENINGOENCEPHALITIS WITHOUT ESCHAR AND DIRECT EXPOSURE HISTORY

Young Ok KIM Department of Pediatrics, Chonnam National University Hospital, Gwangju, Republic of Korea

### P-26

# PATTERNS OF BRAIN LESIONS IN NEONATES WITH HERPES SIMPLEX ENCEPHALITIS

Hiroyuki KIDOKORO Department of Pediatrics, Nagoya University Graduate School of Medicine, Nagoya, Japan

### P-27

#### BARBITURATE COMA THERAPY FOR CHILDREN WITH ACUTE ENCEPHALOPATHY

Yusuke ISHIDA Department of Neurology, Hyogo Prefectural Kobe Children's Hospital, Kobe, Japan

## P-28

# STATUS EPILEPTICUS IN INFLUENZA VIRUS INFECTION AFTER INTRAVENOUS FOSPHENYTOIN ADMINISTRATION WITHOUT PRECEDING BENZODIAZEPINE

Yuji SUGAWARA Department of Pediatrics, Soka Munincipal Hospital, Soka, Japan

## P-29

# TWO UNIQUE CASES OF PYRIDOXAL PHOSPHATE-RESPONSIVE INFANTILE EPILEPTIC ENCEPHALOPATHIES

Yoshiyuki HANAOKA Department of Child Neurology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences and Okayama University Hospital, Okayama, Japan

P-30

#### WEST SYNDROME - A SINGLE CENTRE 5-YEAR REVIEW FROM SINGAPORE

**Hian-Tat ONG** Khoo Teck Puat - National University Children's Medical Institute, National University Hospital, National University Health System, Singapore

## P-31

THE EFFECT OF STEROID PULSE THERAPY ON A CASE OF DRAVET SYNDROMETakako FUJITADepartment of Pediatrics, School of Medicine, Fukuoka University

## P-32

**EPILEPTIC ENCEPHALOPATHY MARKER OF INBORN ERRORS OF METABOLISM** Ashok GUPTA SMS Medical College, Jaipur, India

### P-33

DRUGS INDICATED FOR MITOCHONDRIAL DYSFUNCION AS TREATMENTS FOR ACUTE ENCEPHALOPATHY WITH ONSET OF FEBRILE CONVULSIVE STATUS EPILEPTICS

 Taku OMATA
 Division of Child Neurology, Chiba Children's Hospital, Chiba, Japan

### **P-34**

#### INCREASED FRACTIONAL ANISOTROPHY, A PARAMETER OF DIFFUSION TENSOR IMAGING, REFLECTS REVERSIBILITY OF ACUTE ENCEPHALOPATHY

Shihoko KIMURA-<br/>OHBADepartment of Neurology, Health Science Center, University of New Mexico,<br/>Albuquerque, USA

P-35

# EPILEPTIC ENCEPHALOPATHY WITH CONTINUOUS SPIKE AND WAVE DISCHARGES DURING SLEEP IN A GIRL WITH ATYPICAL ABSENCE

Ying-Chao CHANG Department of Pediatrics, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan



**Invited Lecturers** 

# **Hideo YAMANOUCHI**

## Present Position

Professor, Department of Pediatrics, Saitama Medical University, Japan

## Education

1985 M.D. Mie University School of Medicine, Mie, Japan 1994 Ph.D. Gunma University School of Medicine, Gunma, Japan

## Academic Appointments

1997-1999 Assistant Professor, Gunma University School of Medicine
1999-2004 Lecturer, Department of Pediatrics, Dokkyo Medical University
2004-2009 Associate Professor, Department of Pediatrics, Dokkyo Medical University
2009-present Professor, Department of Pediatrics, Saitama Medical University

## Licensure and Certification

National Medical License in 1985,

Board Certifications in Pediatrics, Child Neurology, Clinical Epileptology and Medical Genetics

## Memberships

The board of directors, Japanese Society of Child Neurology, The councilor, Japan Epilepsy Society The councilor and secretory general, Infantile Seizure Society The delegate, Japanese Pediatrics Society The member, Japan Society of Human Genetics The Affiliate Member, Child Neurology Society, USA The Member, International Child Neurology Association The Corresponding Active Member, American Academy of Neurology, USA

## Research Grant (recent only)

2013-2015 "Deveopmental analysis of voluntary and involuntary movement from fetal period." Grant-in-Aid for Scientific Research on Innovative Areas, The Ministry of Education,Culture,Sports,Science and Technology (MEXT)

2013-2015 Exergy and rhythm environment promoting healthy development, Grant-in-Aid for Scientific Research (B) Japan Society for the Promotion of Science (JSPS)

2015-2016 Primate model development for the approach to regenerative medicine for neonatal hypoxic ischemic encephalopathy, Grant-in-Aid for challenging Exploratory Research, JSPS.

2015- Establishment of clinical guideline for acute encephalopathy and status epilepticus in childhood. Health Labour Sciences Research Grant



# Masashi MIZUGUCHI

#### Present Position

Professor, Department of Developmental Medical Sciences, Graduate School of Medicine, the University of Tokyo, Tokyo, Japan

#### Education

1980	MD, Faculty of Medicine, University of Tokyo,
	Tokyo
1980-1986	Residency in Pediatrics, Tokyo University Hospital and Tokyo Metropolitan
	Fuchu Hospital and Neurological Hospital, Tokyo
1986-1988	Fellow in Pathology, University of Tokyo
1989	PhD, (Dr. of Medical Science), University of Tokyo

#### Academic Appointments

1988-1993 Assistant, Departments of Neuropathology and Pediatrics, the University of Tokyo, Tokyo
1993-1995 Section Chief, Department of Mental Retardation and Birth Defect Research, National Institute of Neuroscience, Tokyo
1996-2004 Associate Professor, Department of Pediatrics, Jichi Medical School, Tochigi
2004-2007 Associate Professor, Department of Pediatrics, the University of Tokyo, Tokyo
2007-Present Professor, Department of Developmental Medical Sciences, the University of Tokyo, Tokyo

### Publication

- 1. Mizuguchi M, Abe J, Mikkaichi K, Noma S, Yoshida K, Yamanaka T, Kamoshita S. Acute necrotising encephalopathy of childhood: a new syndrome presenting with multifocal, symmetric brain lesions. Journal of Neurology, Neurosurgery and Psychiatry 1995; 58(5): 555-561.
- 2. Mizuguchi M, Yamanouchi H, Ichiyama T, Shiomi M. Acute encephalopathy associated with influenza and other viral infections. Acta Neurologica Scandinavica 2007; 115(4): 45-56.
- Sato A, Kasai S, Kobayashi T, Takamatsu Y, Hino O, Ikeda K, Mizuguchi M. Rapamycin reverses impaired social interaction in mouse models of tuberous sclerosis complex. Nature Communications 2012; 3: 1292.
- Shinohara M, Saitoh M, Nishizawa D, Ikeda K, Hirose S, Takanashi JI, Takita J, Kikuchi K, Kubota M, Yamanaka G, Shiihara T, Kumakura A, Kikuchi M, Toyoshima M, Goto T, Yamanouchi H, Mizuguchi M. ADORA2A polymorphism predisposes children to encephalopathy with febrile status epilepticus. Neurology 2013; 80(17): 1571-1576.
- 5. Takanashi JI, Taneichi H, Misaki T, Yahata Y, Okumura A, Ishida YI, Miyawaki T, Okabe N, Sata T, Mizuguchi M. Clinical and radiologic features of encephalopathy during 2011 E coli O111 outbreak in Japan. Neurology 2014; 82(7): 564-572.



## Solomon L. MOSHÉ

Solomon L. Moshé, M.D., is the Charles Frost Chair in Neurosurgery and Neurology, and Professor of Neurology, Neuroscience, and Pediatrics at the Albert Einstein College of Medicine/Montefiore Medical Center in the Bronx, New York. He is also the current Vice Chairman of the Department of Neurology, Director of Child Neurology and Director of Clinical Neurophysiology.



He was the President of the International League Against Epilepsy

(ILAE) from 2009 to 2013. During his presidency, he collaborated closely with the World Health Organization (WHO) governmental and non-governmental agencies to increase the access of care for people with epilepsy. The main goals are to develop individualized treatments today and to prevent and cure epilepsy tomorrow.

Since 1979 his research has focused on understanding the mechanisms underlying age and sex-related differences in epilepsy in humans and animal models. Current research interests include studies on the role of subcortical circuitries involved in the control of seizures as a function of age and sex; the consequences of seizures on the developing brain; the development of models of catastrophic epilepsies; autonomic dysfunction in pediatric neurology disorders and age and sex related maturational patterns of the substantia nigra in health and disease. His laboratory has developed and patented a novel model of human infantile spasms that can be used to identify novel treatments of this devastating condition. In addition to his laboratory research, he is actively involved in several large multicenter studies examining the consequences of prolonged febrile seizures and absence epilepsy.

He has served as President of the American Epilepsy Society (2000-2001) and President of the American Clinical Neurophysiology Society (1996-1997). He is the recipient of several honors and awards, namely Teacher-Investigator Development Award; Jacob Javits Neuroscience Investigator Award from NIH; Michael Prize for Achievement in Epilepsy Research; The American Epilepsy Society Research Award; Ambassador for Epilepsy Award from the International League Against Epilepsy; the Gloor Award from the American Clinical Neurophysiology Society; J.E. Purkyne Honorary Medal in Biomedical Research by the Czech Academy of Sciences; the 2008 Mentor of the Year Award from Albert Einstein College of Medicine; The 2010 Global and Awareness Award from CURE, Citizens United for Research in Epilepsy; the First Saul R. Korey Award in Translational Science and Medicine, Albert Einstein College of Medicine in 2012 . He has authored over 300 publications and mentored numerous scientists and clinicians from around the world in clinical epilepsy and basic science epilepsy-related research.

# Tetsushi YOSHIKAWA

#### Present Position

Professor and Chair, Department of Pediatrics, Fujita Health University School of Medicine

### Education

MD: Mrach/1986, Fujita Health University School of Medicine PhD: March/1992, Fujita Health University School of Medicine Postdoctoral: April/1993-September/1995, Division of Viral

Product, Center for Biologics Evaluation and Research, FDA, Bethesda, MD

#### Academic Appointments

- 1986-1988 Pediatrician, Department of Pediatrics, Fujita Health University Hospital, Toyoake, Aichi, Japan
- 1992-1993 Pediatrician, Department of Pediatrics, Fujita Health University Hospital, Toyoake, Aichi, Japan
- 1993-1995 Visiting Fellow, Assistant Professor, Department of Pediatrics, Fujita Health University School of Medicine, Toyoake, Aichi, Japan
- 1999-2002 Associate Professor, Laboratory of Virology, Research Institute for Disease Mechanism and Control, Nagoya University School of Medicine, Nagoya, Aichi, Japan
- 2002-2010 Associate Professor, Department of Pediatrics, Fujita Health University School of Medicine, Toyoake, Aichi, Japan
- 2010-present Professor and Chair, Department of Pediatrics, Fujita Health University School of Medicine, Toyoake, Aichi, Japan

### Professional Societies

Japan Pediatric Society American Society for Microbiology Japanese Society for Virologists (Director:2016-2018) Japanese Society of Clinical Virology Japanese Society for Pediatric Infectious Diseases (Director:2012-2015) Japanese Society of Vaccinology Scientific Advisory Board of HHV-6 Foundation

#### Editorial

Associate editor of Journal of Medical VirologyMemberships

#### Research Grant

- 1. Grant from the Ministry of Health, Labour and Welfare of Japan (H24-Shinko-003)
- 2. Grant of National Center for Child Health and Development (22A-9).



## Annamaria VEZZANI

Annamaria Vezzani obtained her PhD degree in Neuropharmacology in Milano at the Mario Negri Institure for Pharmacological Research. She spent her post-doctoral period at the Univeristy of Maryland in Baltimore working on the mechanisms of seizures generation in experimental models of epilepsy. Additional postdoctoral periods were done at the Univeristy of Stockholm and at the Karolinska Institute. She was on sabbatical at the Albert Einstein College of Medicine in 2002 in the laboratory of Developmental Epilepsy.



She studies the biochemical and molecular mechanisms involved in the pathogenesis of seizures and in epileptogenesis using experimental models. The present research is focused on the role of neuroactive inflammatory mediators in aberrant neuronal excitability underlying seizures Focus of research is also on the mechanisms of pharmacoresistance. She has published over 160 original papers, several book chapters and reviewes in peer-reviewed high impact scientific journals (h-index 57).

Since 1997 she is Head of the Laboratory of Experimental Neurology in the Department of Neuroscience at the Mario Negri Institute for Pharmacological Research, Milan, Italy.

She is member of the Editorial Board of Epilepsy Res, Epilepsy and Treatments and Neuroscience, and she has been for 8 years Associate Editor of Basic Science for Epilepsia.

She has been appointed of the Chair of the Commission on Neurobiology of International League Against Epilepsy (2005-2009) which is promoting initiatives for improving translational research in epilepsy. She is now liason member of the Commission on Neurobiology and active member of the CEA of the ILAE and various AES committees. She received the Research Recognition Award for translational research in 2009 by the American Epilepsy Society.

## Shinichi HIROSE

#### Present Position

Professor and Chairman, Department of Pediatrics, School of Medicine, Fukuoka University

Director, Center for Maternal, Fetal and Neonatal Medicine, Fukuoka University Hospital

#### Education

1980 M.D. Fukuoka University, School of Medicine

1988 Ph.D. Fukuoka University, School of Medicine (Biochemistry)

Postdoctoral Training:

Residencies:	
1980-1982	Resident, Fukuoka University Hospital
Fellowships:	
1982-1984	Clinical Fellow in Pediatrics, Fukuoka University Hospital

### Academic Appointments

4/1992-9/1992	Associate Physician in Pediatrics, Fukuoka University Hospital
10/1992-3/1994	Instructor in Pediatrics, Fukuoka University Hospital
4/1994-3/1997	Assistant Professor, Department of Pediatrics, School of Medicine
	Fukuoka University
4/1997-3/2005	Associate Professor, Department of Pediatrics, School of Medicine,
	Fukuoka University
4/2006-3/2010	Professor and Chairman, Department of Pediatrics, School of Medicine,
	Fukuoka University
	Director, Center for Maternal, Fetal and Neonatal Medicine, Fukuoka
	University Hospital
4/2006-3/2010	Director, The Research Center for the Molecular Pathomechanisms of
	Epilepsy, Fukuoka University
4/2011-	Director, Central Research Institute for the Molecular Pathomechanisms
	of Epilepsy, Fukuoka University
4/2014	Director, Center for Maternal, Fetal and Neonatal Medicine, Fukuoka
	University Hospital

#### • Awards and Honors:

1998 Fukuoka Prefecture Medical Association Young Investigator Award

- 1999 The Best Paper Award in the 102nd annual meeting of the Japanese Society for Pediatrics.
- 2001 Epilepsy Research Foundation Award
- 2003 Kawano Pediatric Medicine Award
- 2004 The 8th Asian & Oceania Congress of Child Neurology AOCNA Best Presentation Award
- 2013 Korean Epilepsy Congress Best Oral Presentation Award Memberships
- Research Grant (recent only)



## Aristea S. GALANOPOULOU

Professor of Neurology & Neuroscience Albert Einstein College of Medicine Bronx NY, USA aristea.galanopoulou@einstein.yu.edu

Aristea S. Galanopoulou, MD PhD is a Professor of Neurology and Neuroscience at the Albert Einstein College of Medicine in Bronx, NY, USA. Dr Galanopoulou received her MD from National and



Kapodistrian University of Athens, Greece, her PhD from McGill University in Montreal Canada and completed her Neurology and Clinical Neurophysiology training at the Albert Einstein College of Medicine in Bronx NY. She is a clinical epileptologist and also conducts basic epilepsy research using a variety of animal models, particularly models of early life seizures and epilepsies. Specific areas of research interest are: pathogenic mechanisms and consequences of early life seizures, status epilepticus and early life epileptic encephalopathies; development of new therapies using animal models; age and sex specific factors in brain maturation and epilepsy expression; neuroinflammation; GABAA receptor physiology and role in epileptogenesis; Rett syndrome. She has been the author of more than 90 peer-reviewed publications.

She has been an Associate Editor in the three volume book "Atlas of Epilepsies", Guest Editor in two Special Issues on "Sex and Epileptogenesis" (Neurobiology of Disease) and on treatments for Prolonged Epileptic Seizures (Epileptic Disorders). She is Associate Editor of Epileptic Disorders and Epilepsia Open, member of the Editorial Board of Neurobiology of Disease, Epilepsia, CNS Neuroscience and Therapeutics; member of the Editorial Boards for Neurobiology of Disease, Epilepsy Research, CNS Neuroscience & Therapeutics, Epilepsy Research, and Drugs. She is a member of multiple committees within the American Epilepsy Society (AES) and International League Against Epilepsy (ILAE) that work for the optimization of preclinical epilepsy research, education, and therapy development. Dr Galanopoulou is also the co-chair of the AES/ILAE Translational Research Task Force of the ILAE, which works towards the optimization of the use of animal models of seizures, epilepsies, and comorbidities in epilepsy research. In 2015, Dr Galanopoulou received the Ambassador of Epilepsy Award from the ILAE and IBE.

# Jun-ichi TAKANASHI

#### Present Position

Vice-Director, Professor of Pediatrics and Pediatric Neurology, Tokyo Women's Medical University Yachiyo Medical Center, Yachiyo, Japan.

### Education

1998. PhD, (Doctor of Medical Science), Graduate School of Medicine, Chiba University

1988. MD, Chiba University School of Medicine

2001-2002. Radiology, University of California San Francisco (Prof. A. James Barkovich)

### Academic Appointments

- 2014-2015. Associate Professor, Tokyo Women's Medical University Yachiyo Medical Center.
- 2005-2014. Chief of Pediatric Neurology, Kameda Medical Center, Kamogawa, Japan.

1998-2004. Assistant Professor, Department of Pediatrics, Chiba University, Japan.

- 2000-present. Research Associate, Department of Medical Image, National Institute of Radiological Sciences, QST, Inage, Japan.
- 2009-presnt. Visiting Professor, Department of Radiology, Toho University Sakura Medical Center, Sakura, Japan.

### Research Grant (on-going only)

JSPS, KAKENHI (C-16K10329)

### Publication

First author, 61 papers including 8 Neurology, 17 AJNR, coauthor, 73 papers.

Fujita Y, <u>Takanashi J</u>,et al. Activated microglia in acute encephalopathy with biphasic seizures and late reduced diffusion. *J Neurol Sci* 2016; 366: 91-93.

<u>Takanashi J</u>, et al. Disrupted glutamate-glutamine cycle in acute encephalopathy with biphasic seizures and late reduced diffusion. *Neuroradiology* 2015; 57: 1163-1168

<u>Takanashi J</u>, et al. Clinical and radiological features of encephalopathy during 2011 E. coli O111 outbreak in Japan. *Neurology* 2014; 82: 564-572.

Takanashi J, et al. Excitotoxicity in acute encephalopathy with biphasic seizures and late reduced diffusion. Report of 3 cases. *AJNR Am J Neuroraiol* 2009; 30: 132-135.

<u>Takanashi J</u> et al..Diffusion MRI abnormalities after prolonged febrile seizures with encephalopathy. *Neurology* 2006; 66: 1304-1309.

Tada H, <u>Takanashi J</u>, et al. Clinically mild encephalitis/encephalopathy with a reversible splenial lesion. *Neurology* 2004; 63: 1854-1858.



# Akihisa OKUMURA

#### Present position

Professor, Department of Pediatrics, Aichi Medical University

## Office Address

1-1 Yazako Karimata, Nagakute, Aichi, 480-1195 Japan Phone: +81-561-62-3311 Fax: +81-561-63-4835 Email: okumura.akihisa.479@mail.aichi-med-u.ac.jp

## Academic career

Graduated from Nagoya University School of Medicine, 1989 Resident at Tokai Chuo Hospital, 1989-1990 Department of Pediatrics, Nagoya University Hospital, 1991-1992 Department of Pediatrics, Anjo Kosei Hospital 1992-1998 Assistant, Department of Pediatrics, Nagoya University Graduate School of Medicine 1998.4- 2005.10 Assistant professor, Department of Pediatrics, Nagoya University Graduate School of Medicine 2005.11-2006.3 Assistant professor, Department of Pediatrics, Juntendo University Faculty of Medicine 2006.4-2014.1 Professor, Department of Pediatrics, Aichi Medical University 2014.2-present

## Memberships and Activities in Societies

Asian Editor, Neuropediatrics Member of the Board of Trustee, Japanese Society of Child Neurology Japan Epilepsy Society Japan Pediatric Society Infantile Seizure Society Japan Society of Perinatal and Neonatal Medicine



## **Sooyoung LEE**

#### Present Address

5-1-1,kashiiteriha,Higashi-ku,Fukuoka,Japan 813-0017 Tel .+81-92-692-3402 E-mail:lee.s@fcho.jp

## Education

2002 Graduated from Hiroshima University



## Experience

April 2015-Present April 2008-March 2015

Critical Care Medicine, Fukuoka Children's Hospital Emergency and Critical Care Center Kyushu University Hospital

### Licensure and Certification

Japanese Certified Board Pediatrician No 30145 Japanese Certified Board Child neurologist No 24043 Japanese Certified Board Acute care physician No 4726

# Masashi SHIOMI

#### Present Position

Chief, Department of Pediatrics, Aizenbashi Hospital, Osaka, Japan

## Education and assignments

1976:MD, Osaka University School of Medicine

1990:PhD. Research Institute for Microbial Diseases, Osaka University

1980-1993:Division of Pediatrics, Infectious Disease Center, Momoyama Memorial Hospital, Osaka, Japan



1993-2011:Cheif, Division of Pediatric Infectioius Disease and Emergency Peatrics, Pediatric Medical Care Center, Osaka City General Hospital, Osaka, Japan 2011-:Chief, Department of Pediatrics, Aizenbashi Hospital, Osaka, Japan

## Selective publications:

- 1. Shiomi M, Togawa M, Kurimasa H, Kawawaki H, Tomiwa K, Sawada Y, Shintaku H. Neopterin Concentration of serum and cerebrospinal fluid febrile convulsion, aseptic meningitis and influenza encephalopathy. Pteridines.1999;10:35-38
- 2. M.Shiomi. An attempt at clical classification of influenza encephalopathy. Japanese Journal of Pediatrics 2000;53:1739-1746 (in Japanese)
- 3. M.shiomi, Ishikawa J, Togawa M, Okazaki S, Kuki I, Kimura S, Kawawaki H. Acute encephalopathy with febrile convulsive status epilepticus: description of AEFCSE and theophylline as one of its causative agents. No to Hattatsu 40:122-127,2008(in Japanese)
- 4. Shiomi M. The Classification of Acute encephalitis and Acute encephalopathy. In Igarashi T, Shiomi M, eds. The compass for clinical pediatrics. Acute encephalitis and acute encephalopathy. Nakayama Shoten, Tokyo, 2011 (in Japanese)

# I-Jun CHOU

## Current Position

Chief, Department of Paediatric Neurology, Division of Paediatrics, Chang Gung Memorial Hospital

Department of Paediatric Neurology, Division of Paediatrics, Chang Gung Memorial Hospital

## Address

5. Fu-hsing street. Kuei shan hsiang, Taoyuan hsien, Taiwan, R.O.C. TEL :+886-3-3281200 ext 8200

E-Mail: ijun@adm.cgmh.org.tw; chouijun@gmail.com

## Eudcation

- 2001 M.D. Chang-Gung University (CGU), Taiwan
- 2011-2016 PhD candidate, Clinical Neurology, School of Clinical Sciences, University of Nottingham, UK

### Previous Post

- 2009-2011 Honorary research fellow, Academic Division of Clinical Neurology, School of Medicine, University of Nottingham, UK
- 2009-2011 Attending Physician, Pediatric department, Chang Gung Memorial Hospital, Taiwan
- 2008-2009 Attending Physician, Pediatric department, NanMen General Hospital, Taiwan
- 2007-2008 Attending Physician, Pediatric department, Chang Gung Memorial Hospital, Taiwan

### Licensure and Certification

- 2010 Board Certification in Pediatric Emergency Medicine, Taiwan
- 2007 Board Certification in Pediatric Neurology, Taiwan
- 2005 Board Certification in Pediatric Medicine, Taiwan
- 2001 Diplomate, National Board of Medical Examiners, Taiwan

## Teaching Activities

2014 -- Assistant Professor, Chang Gung Memorial Hospital, Linko branch, Taoyuan, Taiwan

2009-2013 Lecturer, Chang Gung Memorial Hospital, Taoyuan, Linko branch, Taiwan Research Project

- 2012-2015 Correlative Study of Clinical, Imaging, and Immunology Features of Acute Central Nervous System Inflammatory Demyelinating Syndromes; Chang Gung Memorial Hospital CMRP grant, Taiwan
- 2010-2011 Screening of serum anti-neuronal autoantibodies in children and adolescents with post-encephalitic epilepsy; Chang Gung Memorial Hospital CMRP grant, Taiwan
- 2010-2012 Quantitative analysis of serum anti-neuronal autoantibodies in children and adolescents with post-encephalitic epilepsy; Chang Gung Memorial Hospital CMRP grant, Taiwan
- 2009-2011 Survival impact of gout and hyperuricaemia
- 2007-2008 Association between Tourrette Syndrome and Group A Streptococcus Infection, Taiwan



# Hitoshi OSAKA

#### Present Position

Professor, Jichi Medical Univ., Dept of Pediatrics

### Postdoctoral Training

- 1987-1989 Junior Resident, Kanagawa Children's Medical Center, Yokohama
- 1989-1996 Medical staff, Neuropediatric division, Department of Pediatrics, Yokohama City University School of Medicine, Yokohama



- 1996-1999 Postdoctral fellow, Department of Pharmacology, School of Medicine, University of California, San Diego, CA
- 1999-2002 Research fellow, Department of Degenerative Neurological Diseases, National Institute of Neuroscience, National Center of Neurology and Psychiatry
- 2002- Investigator of Information and Cellular function, PRESTO, Japan Science and Technology Corporation (JST)
- 2003- Stuff of Neurology, Kanagawa Children's Medical Center
- 2009- Chief of Neurology, Kanagawa Children's Medical Center
- 2012- Visiting Professor, Yokohama City Univ. School of Medicine
- 2014- Professor, Jichi Medical Univ., Dept of Pediatrics

### Licenser and Certification

- 1987 National Board of Medicine
- 1992 Japanese Board of Pediatrics
- 1992 Japanese Board of Child Neurology
- 2009 Japanese Board of Epilepsy

### Memberships

Japan Pediatric Society, Japanese Society of Child Neurology, Societas Neurologica Japonica, Japanese Society of Epilepsy, Japanese Society of Inherited Metabolic Diseases, Japanese Society of Molecular Genetics, Japanese Society of Biochemistry, Editorial Board.World Journal of Medical Genetics

### Fellowships

1996-1997Rotary International Fellowship1997-1998Uehara Memorial Fellowship

### Councilor

Japanese Society of Pediatrics, Japanese Society of Epilepsy Japanese Society of Pediatric Neurology, Japanese Society of Biochemistry

## Grants

2005-	Research Grants from the Ministry of Health, Labor, and Welfare, Japan
2005-	Grant for Kanagawa children's hospital
2008-	Yokohama Foundation for Advancement of Medical Science
2011-	Grants-in-aid for scientific research (kiban C, B) from the Ministry of
	Education, Culture, Sports, Science, and Technology, Japan

# Yushiro YAMASHITA

### Current position

Professor and Chairman

Department of Pediatrics & Child Health, Kurume University School of Medicine, Fukuoka, Japan

## Education, Academic appointments

1983:	M.D., Kurume University School of Medicine
1983-84	Resident in Pediatrics, Kurume University Hospital
1987:	Ph.D., Kurume University School of Medicine
1989:	Short-term expert on Pediatric Neurology, Islamabad Children Hospital,
	Pakistan (JICA)
1990-1993:	Research associate at Pediatric Neurology, Baylor College of Medicine,
	Houston TX, USA
2003:	Fellowship at the State Univ. NY at Buffalo (Recipient of Eli Lilly
	Fellowship Award)
2013:	Professor, Division of Developmental Disorders, Department of Pediatrics &
	Child Health, Kurume University School of Medicine
2015:	Present position

### Main research field

Developmental disorders (ADHD, Rett syndrome, ASD, LD)



# Philip L. PEARL

#### Present Position

William G. Lennox Chair in Pediatric Epilepsy, Director of Epilepsy and Clinical Neurophysiology

#### Education

06/1984 MD, University of Maryland, Baltimore, MD

- 06/1986 Residency, Pediatrics, Baylor College of Medicine, Houston, TX
- 06/1989 Residency, Neurology and Child Neurology, Baylor College of Medicine, Houston, TX
- 06/1990 Fellowship, Clinical Neurophysiology, Boston Children's Hospital, Harvard Medical School, Boston

#### Positions and Employment

- 1997 Special Volunteer, Clinical Epilepsy Branch, Office of the Clinical Director, Division of Intramural Research, NINDS, NIH, Bethesda, MD
- 2006 Visiting Associate Professor, Pediatrics, University of Virginia School of Medicine, Charlottesville, VA
- 2014 William G. Lennox Chair and Professor of Neurology, Harvard Medical School, Boston, MA
- 2014 Director, Epilepsy and Clinical Neurophysiology, Boston Children's Hospital, Boston, MA

#### Other Experience and Professional Memberships

- 2001 Pediatric Neurotransmitter Diseases Association, Medical and Scientific Advisory Board
- 2003 Committee for Part I Written Examination, American Board of Psychiatry and Neurology
- 2003 Chairman, Awards Committee, Child Neurology Society
- 2007 Secretary-Treasurer, Professors of Child Neurology
- 2008 FDA Public Advisory Committee on Antiepileptic Drugs
- 2012 2014 President, Professors of Child Neurology
- 2013 Vice Chair, Child Neurology Section, American Academy of Neurology

#### Personal Statement

My research focus is metabolic epilepsy and the pediatric neurotransmitter disorders, specifically disorders of GABA metabolism. Over the past 13 years, I have studied succinic semialdehyde dehydrogenase (SSADH) deficiency, in collaboration with K. Michael Gibson, PhD, who developed the mouse model. I have maintained a longitudinal natural history database of the condition and have reported on the clinical, imaging, and neurophysiologic features of the disorder. I have and continue to receive federal funding (NINDS R01 HD58553 and R01 NS 82286) utilizing biomarkers and clinical trials in this disorder. Following a nearly 17 year history at Children's National Medical Center from 1997–2013, during which I became Division Chief of Child Neurology and served as Neurology Program Director at Children's National and the Director of Medical Student Education in Neurology at George Washington University School of Medicine, I was recruited to the William G. Lennox Chair in Pediatric Epilepsy and Director of Epilepsy and Clinical Neurophysiology at Boston Children's Hospital as of January 2014. Currently, I am a member of the Neurology Residency Review Committee of the ACGME and am Past President of the Professors of Child Neurology, the national organization representing academic pediatric neurology. In the current proposal, I will serve as a clinical investigator, and will facilitate patient recruitment, aid in the establishment of clinical goals, and interpret results in the context of individual clinical profiles.



# Hsiu-Fen LEE

#### Present Position

Attending Physician, Department of Pediatrics, Taichung Veterans General Hospital Assistant Professor, College of Medicine, Chung-Shan Medical University, Taichung, Taiwan,

#### Address

1650, Taiwan Boulevard Sec. 4, Taichung, 407, Taiwan Phone: 886-4-23592525 ext 5976 Fax; 886-4-23741359 E-mail: leehf@hotmail.com.tw

#### Certification

- 1996 Medical Doctor, Taiwan
- 1999 Pediatrics, Taiwan
- 2001 Child Neurology, Taiwan
- 2010 Ph.D.,

#### Academic Background

- 2004-2010 Institute of Biochemistry and Biotechnology, College of Medicine, Chung-Shan Medical University, Taichung, Taiwan,
- 2004- Attending Physician, Department of Pediatrics, Taichung Veterans General Hospital, Taichung, Taiwan,
- 1999-2004 Fellowship of Pediatric Neurology, Taichung Veterans General Hospital, Taichung, Taiwan,
- 1996-1999 Resident, Department of Pediatrics, Taichung Veterans General Hospital, Taichung, Taiwan,
- 1989-1996 College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan,

### • Selected publications in recent five years (\*: Corresponding author)

- 1. Liaw HR, Lee HF, Chi CS\*, Tsai CR. Late infantile metachromatic leukodystrophy: Clinical manifestations of five Taiwanese patients and genetic features in Asia. Orphanet J Rare Dis 2015; 10:144. (Liaw and Lee equally contributed to this work.)
- 2. Lee HF, Chi CS\*, Tsai CR, Chen CH, Wong CC. Electroencephalographic features of patients with SCN1A-positive Dravet syndrome. Brain Dev 2015;37:599-611
- 3. Lee HF, Chi CS\*. Enterovirus 71 infection-associated acute flaccid paralysis: A case series of long-term neurologic follow-up. J Child Neurol 2014; 29:1283-1290
- 4. Chi CS, Lee HF\*, Tsai CR. Tyrosine hydroxylase deficiency in Taiwanese infants. Pediatr Neurol 2012;46:77-82.
- 5. Lee HF, Chi CS\*, Jan SL, Fu YC, Huang FL, Chen PY, Wang CC, Wei HJ. Extracorporeal life support for critical enterovirus 71 rhombencephalomyelitis: long-term neurologic follow-up. Pediatr Neurol 2012;46:225-230.
- 6. Lee HF, Chi CS\*, Tsai CR, Chen CH. Epileptic seizures in infants and children with mitochondrial diseases. Pediatr Neurol 2011;45:169-174.



# **Russell C. DALE**

#### Present Position

Professor of Paediatric Neurology, University of Sydney Head, Institute for Neuroscience and Muscle Research Paediatric Neurologist, the Children's Hospital at Westmead

## Education

MBChB University of Leeds, UK 1992 MCRP, MRCPCH Royal College of Paediatrics and Child health, 1995 MSc, University of London, 2000 PhD, University of London 2006

### Academic Appointments

Professor of Paediatric Neurology SubDean Research, Discipline of Child and Adolescent Health, University of Sydney

### Licensure and Certification

Royal College of Paediatrics and Child Health UK Royal Australian College of Physicians

#### Memberships

Australia New Zealand Child Neurology Society British Paediatric Neurology Association International Child Neurology Association

### Research Grant (on-going only)

National Health Medical Research Council Practitioner Fellowship "Early Identification and Treatment of Autoimmune Brain disease in children" 2014-2018 National Health Medical Research Council Project Grant "Autoimmune movement disorders in children" 2015-2017 Multiple Sclerosis Research Australia Project Grant " Myelin Oligodendrocyte

Glycoprotein Autoantibodies in CNS demyelination" 2015-2016

#### Publication

160 peer reviewed publications, mostly in neuroimmunology and movement disorders. Web of science 3850 citations (655 in 2016)- H factor 34. Google Scholar 5900 citations (920 in 2016)- H factor 44.

Most publications focus on clinical phenomenology of immune mediated CNS disease in children and treatment of these conditions.



# Hiroyuki TORISU

#### Professional address

2-15-1, Tamura, Sawara-ku, Fukuoka 814-0193, JAPAN TEL: +81-92-801-0411 FAX: +81-92-801-3673 torisu@college.fdcnet.ac.jp

## Education

- 1989 B.S., Graduate School of Mathematical Sciences, the University of Tokyo
- 1996 M.D., Faculty of Medicine, Kyushu University
- 2004 Ph.D. in Medicine, Graduate School of Medicine, Kyushu University

## Professional Experience

1999-2000	Clinical Fellow, Division of Child Neurology, Tottori University
2000-2006	Clinical Fellow, Department of Pediatrics, Kyushu University
2006-2010	Assistant Professor, Department of Pediatrics, Kyushu University
2010-2015	Lecturer, Department of Pediatrics, Kyushu University
2015-present	Associate Professor, Section of Pediatrics, Department of Medicine,
	Fukuoka Dental College

### Board Certification

- 2002 Japan Pediatric Society
- 2004 The Japan Society of Child Neurology
- 2014 The Japan Epilepsy Society

## Society Membership

Japan Pediatric Society, The Japan Society of Child Neurology,

The Japan Epilepsy Society, Japanese Society for Neuroinfectious Diseases, The Japanese Society for Neuroimmunology



# Yukitoshi TAKAHASHI

#### Present Position

Vice-director, National epilepsy center, Shizuoka institute of epilepsy and neurological disorders, NHO. Clinical Professor, Department of pediatrics, Gifu University School of Medicine, and Visiting Professor School of Pharmaceutical Sciences, University Shizuoka, Japan.



Dr. Takahashi has MD from Gifu University. He started the study about photosensitive mechanisms from 1991, and autoimmunity in epilepsy and encephalitis from 2000 in collaboration with Prof Mishina of Tokyo University, and published many papers concerning about photosensitivity, Rasmussen syndrome, epilepsy after acute encephalitis, and acute encephalitis. He is a member of board of Japan Neuroinfection Society: member of board of Japan Epilepsy Society; member of pharmaceutical committee of Japan Child Neurology Society; and member of board of Japan Society of Human Genetics. He received JUHN and MARY WADA Award from Japan Epilepsy Society, Japanese Society for Neuroimmunology Award, 10th Kawano Prize, The Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology, and Research award of Japan Pediatric Society. His main research interests include: Mechanisms and pathogenesis of neuroimmunological diseases, particularly non-paraneoplastic acute limbic encephalitis, Rasmussen encephalitis, and epilepsy after acute encephalitis, Rasmussen encephalitis, and epilepsy after acute encephalitis, photosensitive epilepsy.

## Selected Publications in the field of immune-mediated encephalitis & epilepsy

- 1. T Fukuyama, Y Takahashi, et al., Semi-quantitative analyses of antibodies to N-methyl-D-aspartate type glutamate receptor subunits (GluN2B & GluN1) in the clinical course of Rasmussen syndrome, Epilepsy Res. 2015; 113: 34-43.
- 2. T Armangue, Takahashi Y, et al., A novel treatment-responsive encephalitis with frequent opsoclonus and teratoma. Ann Neurol. 2014; 75(3): 435-41.
- 3. Y Takahashi, et al., Genetic variations of immunoregulatory genes associated with Rasmussen syndrome. Epilepsy Research, 2013; 107: 238-243.
- 4. Y Takahashi, et al., Immunomodulatory therapy versus surgery for Rasmussen syndrome in early childhood, Brain & Development, 2013; 35: 778-785.
- 5. Y Takahashi, et al., A substantial number of Rasmussen syndrome patients have increased IgG, CD4+ T cells, TNF  $\alpha$ , and Granzyme B in CSF, Epilepsia, 2009; 50: 1419-1431.
- 6. Y Takahashi, et al., Autoantibodies to NMDA receptor in patients with chronic forms of epilepsia partialis continua. Neurology 2003; 61(7):891-896. Oct14]
- 7. Y Takahashi, et al., Optical filters inhibiting television-induced photosensitive seizures. Neurology 2001; 57: 1767-1773.



## Pratibha SINGHI

Prof. Singhi is currently Senior Professor and Head Department of Pediatrics and Chief, Pediatric Neurology and Neuro-Development in the Advanced Pediatrics Centre, Post Graduate Institute of Medical Education and Research Chandigarh. She is also the Honorary Chief Consultant at Prayas – the Rehabilitation Centre for Disabled children, Chandigarh since 1985. She has also worked as locum consultant Neurologist at the Great Ormond Street Hospital, London in 2005 and 2008.

She did her MD Pediatrics from All India Institute of Medical Sciences, New Delhi and received training in Pediatric Neurology, Epilepsy and



Developmental Pediatrics at Johns Hopkins Hospital Baltimore, USA, and at the Kennedy Krieger Institute Baltimore, USA and at Royal Hospital for Sick Children Edinburgh, and at the Royal Victoria Infirmary, Newcastle Upon Tyne, UK.

She has done original research in the field of CNS infections, Neuro-developmental disorders and epilepsy. She has conducted several research projects including those from WHO, ICMR, ICSSR, PGI, and INDO UK collaborative project on neurocysticercosis, INDO-EU Project on NCL and an INDO-Swedish Project on CNS Infections.

She has over 300 research publications and has written / edited 3 books including the ICNA book on CNS Infections. She has been an invited speaker in over 300 conferences. She is an editorial board member, guest editor and reviewer of several international and national journals. She has received several research awards including the James Flett Gold Medal of IAP, Asian Research Award 6th Infantile Seizure Society at Tokyo, Medical Scientist Award and the first S. Janaki Memorial Oration of the National Academy of Medical Sciences, for her outstanding contribution to Pediatric Neurology. Recently her collaborative work on CNS infections with the PICU team was awarded the "research paper of the year" by the BMJ South Asia Awards. She has received several international and national fellowships including Rotary International Foundation Graduate Fellowship, University of Southern California Los Angeles- U.S.A, Heinz Fellowship of the British Pediatric Association in Pediatric Neurology, Epilepsy and Neuro-Development at (i) The Royal Hospital for Sick Children Edinburgh, UK and (ii) The Royal Victoria Infirmary New Castle-U.K., WHO Fellowship Thailand & Nepal, Fellowship in Pediatric Neurology and Epilepsy at Johns Hopkins Hospital and Neuro-Development at Kennedy Krieger Institute, Baltimore- USA in 1991-92, Fellowship of the Royal College of Pediatrics and Child health London UK 2000-for Pediatric Epilepsy and Neurology, Fellowship of Indian Academy of Pediatrics, Fellowship of National Academy of Medical Sciences. She has been visiting professor to prestigious universities in India and abroad including Nehru Chair Visiting Professorship M.S. University Baroda, Karolinska Institute, Stockholm, Sweden and Hospital for Sick Kids, Toronto. Dr. Singhi received several Gold Medals including the President of India Medal for her academic achievements.

Dr. Singhi is also a Task Force / Advisory Board Member in various councils including Expert Group Member World Bank Core group for integrated child development multisectoral research, Member National Advisory Council Institute of Mental Handicap Secunderabad, Expert Group Member National Institute of Mental Handicap Secunderabad for development of Indian Scale for Autism, Member National Advisory Council Centre for Early Childhood Education and Child Development.

Prof Singhi has been a founder member of Child Neurology in India. She was the National President of the Association of Child Neurology India and Vice President Indian Academy of Cerebral Palsy. She is the National Delegate from India for the Asian Oceanian Association of Child Neurology and is a member of the Executive Board and life member of the International Child Neurology Association. She is Fellow and Life member of Indian Academy of Pediatrics, Fellow and Life member of National Academy of Medical Sciences, Executive Board Member International Child Neurology Association (ICNA), Asian Oceanian Child Neurology Association (AOCNA), International Society for Behaviour and Development, Indian Academy of Neurology, National Academy of Medical Sciences, and has held many executive offices of the Indian Academy of Pediatrics. She is an active life member of Indian Council for Child Welfare and has crusaded for the cause of children with special needs.

# **Pin Fee CHONG**

#### Present Position

Department of Pediatric Neurology, Fukuoka Children's Hospital Department of General Pediatrics & Interdisciplinary Medicine, Fukuoka Children's Hospital

## Education and Training

2006	Kyushu University, School of Medicine, Fukuoka:
	MD, Medicine
2006-2008	Internship in Medicine, Fukuoka Tokushukai Hospital
2008-2011	Residency in Pediatrics, Fukuoka Tokushukai Hospital
2011-2014	Residency in Child Neurology, Fukuoka Children's Hospital
2014 -	Current position

## Certified Board Member

Japan Pediatric Society Japanese Society of Child Neurology



## Raman SANKAR

#### Present Position

Professor of Neurology and Pediatrics and Chief of Pediatric Neurology at the David Geffen, School of Medicine at the University of California, Los Angeles, CA, USA

#### Education

1968-1974	Ph.D., University of Washington, Seattle, Washington
1982-1986	M.D., Tulane Medical School, New Orleans,
	Louisiana
1986-1988	Pediatric Intern-Resident, Children's Hospital of Los Angeles
1988-1989	Resident, Department of Neurology, UCLA School of Medicine,
	Los Angeles, CA
1989-1991	Fellow, Division of Pediatric Neurology, ditto

#### Appointments

1992-1999	Assistant Professor, UCLA School of Medicine
1999-2005	Associate Professor, Director of Residency Training in Child Neurology,
	David Geffen School of Medicine at UCLA
2005-	Present Professor and Chief, Rubin Brown Distinguished Chair Division of
	Pediatric Neurology, David Geffen School of Medicine at UCLA

### Selected Publications

- 1. Sankar R, Curran JG, Kevill J, Rintahaka PJ, Shewmon DA, Vinters HV. Microscopic cortical dysplasia in infantile spasms: evolution of white matter abnormalities. AJNR Am J Neuroradiol 1995; 16:1265-72.
- Sankar R, Shin DH, Liu H, Mazarati AM, Pereira de Vasconcelos A, Wasterlain CG. Patterns of status epilepticusinduced neuronal injury during development and long-term consequences. J Neurosci 1998; 18: 8382-93.
- 3. Sankar R, Shin DH, Mazarati AM, Liu H, Katsumori H, Lezama R, Wasterlain CG. Epileptogenesis following status epilepticus refl ects age- and model-dependent plasticity. Ann Neurol 2000; 48: 580-9.
- Mazarati AM, Shin D, Kwon YS, Bragin A, Pineda E, Tio D, Taylor A, Sankar R. Elevated plasma corticosterone level and depressive behavior in experimental temporal lobe epilepsy. Neurobiol Dis 2009; 34: 457-61.
- Auvin S, Mazarati A, Shin D, Sankar R. Inflammation enhances epileptogenesis in the developing rat brain.

Neurobiol Dis 2010; 40:303-310.



# **Rima NABBOUT**

#### Current position

-Professor of Paediatric Neurology, Paris Descartes University - Director of the National Centre for Rare Epilepsies, Necker Enfants Malades Hospital, Paris, France

- Research and Academic position position, INSERM U1129 "epilepsy in childhood and brain plasticity", University Paris Descartes, Paris, France.

#### Professional address

Department of Child Neurology and metabolic diseases Necker-Enfants malades hospital, 149 rue de Sèvres, 75015 Paris, France. Tel: 00 33 1 44 38 15 36 Fax: 00 33 1 42 19 26 92 e-mail: rima.nabbout@aphp.fr, rimanabbout@yahoo.com

### Education

Medical Doctor, University Saint Joseph, Beirut, Lebanon, 1990 Pediatrics board, University Saint Joseph, Beirut, Lebanon, 1996 MD degree and Pediatric board, University Paris Descartes, Paris 5, France, 2000 Master in Neurosciences, University Pierre et Marie Curie, Paris 6, France, 2000 PhD in Neurosciences, University Pierre et Marie Curie, Paris 6, France, 2003 Habilitation for Direction of Research, University Pierre et Marie Curie, France, 2010

### Research activity

- Phenotyping epilepsy syndromes
- Identifying genetic basis and underlying mechanisms of epileptic syndromes.
- Childhood epilepsies therapies.

#### Peer reviewed articles

Over 120 peer reviewed papers in the field of epilepsies (Nabbout R, PubMed)

#### National and International conferences

Regular speaker (invited speaker or original presentation) to National, European and International conferences of Child Neurology and Epilepsy Editorial responsibilities: Member of the editorial board of Epilepsia

#### Reviewer for

Nature Genetics, Lancet Neurology, Annals of Neurology, Brain, Neurology, Neurobiology of diseases, Epilepsia, Pediatrics, Epilepsy Research, Seizures, American Journal of Human Genetics, European Journal of Human Genetics, American Journal of medical Genetics, Neurogenetics, European Journal of medical Genetics, European journal of Neurology, European Journal of Pediatric Neurology



# Hiroshi SAKUMA

#### Present Position

Project Leader, Developmental Neuroimmunology Project, Department of Brain Development and Neural Regeneration, Tokyo Metropolitan Institute of Medical Science

#### Education

1987–1993 Tokyo Medical and Dental University, Faculty of Medicine



- 1997–1998 Dept. of Pediatrics, Tokyo Medical and Dental University Hospital
- 1998–2000 Resident in Child Neurology, National Center Hospital for Mental, Nervous and Muscular Disorders, National Center of Neurology and Psychiatry
- 2003–2005 Research Associate, Dept. of Molecular Neuropathology, Tokyo Metropolitan Institute for Neuroscience
- 2007–2010 Attending Physician, Dept. of Child Neurology, National Center of Neurology and Psychiatry
- 2010–2012 Postdoctoral Fellow, Dept. of Immunology, National Institute of Neuroscience, National Center of Neurology and Psychiatry
- 2012–2015 Senior Researcher, Mental Development Project, Tokyo Metropolitan Institute of Medical Science
- 2015– Project Leader, Developmental Neuroimmunology Project, Tokyo Metropolitan Institute of Medical Science

## Selected Publications

- 1. Nakahara E, Sakuma H, Kimura-Kuroda J, et al. A diagnostic approach for identifying anti-neuronal antibodies in children with suspected autoimmune encephalitis. J Neuroimmunol 2015:285:150-5.
- 2. Sakuma H, Tanuma N, Kuki I, et al.. Intrathecal overproduction of proinflammatory cytokines and chemokines in febrile infection-related refractory status epilepticus. J Neurol Neurosurg Psychiatr 2015;86:820-2.
- Noto D & Sakuma H (double first authors), Takahashi K, et al. Development of a Culture System to Induce Microglia-like Cells from Haematopoietic Cells. Neuropathol Appl Neurobiol 2014 40:697-713.
- 4. Sakuma H, Awaya Y, Shiomi M, et al. Acute encephalitis with refractory, repetitive partial seizures (AERRPS): a peculiar form of childhood encephalitis. Acta Neurol Scand. 2010;121:251-6.
- 5. Sakuma H. Acute encephalitis with refractory, repetitive partial seizures. Brain Dev. 2009;31:510-4.
- 6. Sakuma H, Kohyama K, Park IK, et al. Clinicopathological study of a myelin oligodendrocyte glycoprotein-induced demyelinating disease in LEW.1AV1 rats. Brain. 2004;127:2201-13.



## Nicola SPECCHIO

#### Nicola Specchio, DOB 5th of December 1974

In 1999 I graduated in Medicine at the University of Bari, Bari, Italy. Research collaboration started in 1994 when I intermittently attended the Institute of Pharmacological Research "Mario Negri", Milano for the study: "Risk in Epilepsy Study Group". Between 1999 and 2004 I trained as a Neurologist at the Neurological Institute of the University of Bari, attending the general neurological ward, the Centre for the Study and Treatment of Epilepsy and the



laboratory of neurophysiology. In 2000 I attended the King's College Hospital, London as research fellow where I participated to outclinic patients and epilepsy surgery meetings. In 2001 I attended the "Neuroscience Unit, Institute of Child Health and Great Ormond Street Hospital for Children, University College London" as research fellow. In 2004 I enrolled for a PhD course in Neuroscience at the "Department of Neurological and Psychiatric Science, University of Bari, Italy. In the same year I started my collaboration with Bambino Gesù Children's Hospital, IRCCS in Rome as Research Fellow under the supervision of Professor Federico Vigevano. During the years spent in Rome the research has been focused on classification and definition of epileptic syndromes, on genetics of epilepsy and epileptic encephalopathies. He has been particularly interested in idiopathic focal epilepsy. Working with professor Vigevano and his research group, he has also been exposed to genetic studies in families with idiopathic focal epilepsies, in the classification of epileptic syndromes and in the characterization of new epileptic syndromes such as Febrile Infection related epileptic syndromes (FIRES) and in PCDH19 related epilepsy syndromes (see published papers). From 2008 to 2013 I had a Full position as a Consultant at Division of Neurology, Bambino Gesu Children Hospital, Roma. Between 2009 and 2011 I attended the Master in Epileptology of the University of Ferrara, Italy. Between 2012 and 2013 I attended with success the Executive Master in Healthcare & Pharmaceutical Administration (EMPHA), University LUISS Guido Carli, Business School, Italy. From the 2011 I am tutor for the Virtual Epilepsy Academy (VIREPA) of the International League Against Epilepsy leading the course on non-epileptic paroxysmal disorders. I contributed with academic lectures to several International Courses on Epilepsies and with the organization of the International Course on Drug Resistant Epilepsies – endorsed by the Commission of European Affair - that is held yearly in Italy in Tagliacozzo (AQ).

From 2014 I am Head of Epilepsy Surgery Unit at Department of Neuroscience, Bambino Gesu Children's Hospital.

I participated as invited speaker to several national and international congresses and workshops, and more recently to the 10th and 11th European Congress of Epilepsy (ECE) and to the 31st International Epilepsy Congress (IEC)

For the period 2011-2014 and 2014-2017 I was elected to the Board of Directors of the Italian League Against Epilepsy.

I actively participated to national and international research projects. I am Author/ coauthor of 85 articles published in International scientific journals, 8 book chapters. Current h-index: 21. I am habitual reviewer for the following journals: Epilepsia, Epilepsy Research, Brain Development, European Journal Neurology, European Journal of Paediatric Neurology, Epileptic Disorders.

# **Judith Helen CROSS**

#### Present Position

The Prince of Wales's Chair of Childhood Epilepsy (since 2008) & Deputy Head of Developmental Neurosciences Programme, Department of Clinical Neurosciences, UCL-Institute of Child Health, University College London

#### Address

UCL-Institute of Child Health, 30 Guilford St, London WC1N 1EH h.cross@ucl.ac.uk

### Current roles

2010-present Chair, BPNA Education Committee

- 2012-present Clinical Advisor, National Childrens Epilepsy Surgery Service
- 2013-2017 Secretary General International League Against Epilepsy
- 2015-present Member, Paediatric Medicines Expert Advisory Group, MHRA

### Relevant publications (10 of total 235)

- 1. Neal EG, Chaffe HM, Edwards N, Lawson M, Schwartz R, Fitzsimmons G, Whitney A, Cross JH A randomised trial of classical and medium chain triglyceride diets in the treatment of childhood epilepsy Epilepsia 2009;50:1109-1117
- Arzimanoglou A ; French J, Blume WT, Cross JH, Ernst JP; Feucht M, Genton, P; Guerrini R, Kluger G, Pellock J, Perucca E, Wheless JW, Lennox-Gastaut syndrome: a consensus approach on diagnosis, assessment, management, and trial methodology. Lancet Neurology, 2009;8:82 – 93
- 3. Cross JH Neurodevelopmental effects of AEDs Epilepsy Research 2010;88:1-10
- 4. Berg AT, Berkovic SF, Buchhalter J, Engel J Jr, Glauser TA, Nordli D, Plouin P, Ryvlin P, Scheffer IE, von Emde Boas W, French J, Cross JH, Mathern GW, Ottman R, Wolf P, Moshe SL, Brodie M.. Report of the Commission on Classification and Terminology: Update and recommendations. Epilepsia 2010;51:676-685
- 5. Skirrow C, Cross JH, Cormack F, Harkness W, Vargha-Khadem F, Baldeweg T. Longterm outcome after temporal lobe surgery in childhood: intellectual gains are correlated with brain volume change. Neurology 2011;76:1330-1337
- D'Argenzio L, Colonelli MC, Harrison S, Jacques TS, Harkness W, Scott RC, Cross JH. Cognitive outcome after extratemporal epilepsy surgery in childhood Epilepsia 2011;52:1966-1972
- 7. Hancock EC, Cross JH. Treatment of Lennox-Gastaut syndrome. Cochrane Database of Systematic Reviews 2012, Issue 3. Art. No.: CD003277.
- Eltze CM, Chong WK, Cox T, Whitney A, Cortina-Borja M, Chin RFM, Scott RC, Cross JH A population based study of newly diagnosed epilepsy in children in the first two years of life Epilepsia 2013;54:437-445
- Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger C, Engel JJ, Jr, French JA, Glynn M, Hesdorffer DC, Lee B-I, Mathern G, Moshé SL, Perucca E, Scheffer IE, Tomson T, Watanabe M, Wiebe S. An Operational Clinical Definition of Epilepsy Epilepsia 2014;55:475-482
- Skirrow C, Cross JH, Harrison S, Cormack F, Harkness W, Coleman R, Meierotto E, Gaiottino J, Vargha-Khadem F, Baldeweg T.Temporal lobe surgery in childhood and neuroanatomical predictors of long-term declarative memory outcome Brain 2015 Jan;138(Pt 1):80-93



## **Kuang-Lin LIN**

#### Present Position

Deputy Chief, Department of Pediatrics, Chang Gung Children Medical Center

## Professional Affiliations

- 1. Chinese Taipei Pediatric Association
- 2. The Society of Ultrasound in medicine, ROC (SUMROC)
- 3. Neurological Society R.O.C.(Taiwan)
- 4. Endocrinological Society R.O.C.(Taiwan)
- 5. Taiwan Child Neurology Society (TCNS)
- 6. Taiwan Epilepsy Society
- 7. American Institute of Ultrasound in Medicine
- 8. Dancing Note--The Association of Children Development
- 9. Taiwan Tourette Association
- 10. The Society of Ultrasound in medicine, ROC (SUMROC)

### Professional activities

- 1. Chief, Division of Neurology, Department of Pediatrics, Chang Gung Children's Hospital, Linko (October 1, 1999-June 2015)
- 2. Director, Dancing Note--The Association of Children Development (July, 1999-2015)
- 3. Director, Taiwan Tourette Association (July 2002-2015)
- 4. President, Taiwan Tourette Association (2010-2014)
- 5. General Secretary of Taiwan Child Neurology Society (TCNS) (2011-2014)
- 6. Director, Taiwan Child Neurology Society (TCNS) (May 2008-2015)

Publications (recent 5 of total 110)

- 1. Lin JJ, Hsia SH, Wang HS, Chiang MC, Lin KL\*. Transcranial Doppler ultrasound in therapeutic hypothermia for children after resuscitation. Resuscitation. 2015 Feb 4;89C:182-187.
- 2. Lin JJ, Lin KL\*, Chan OW, Hsia SH, Wang HS, and the CHEESE Study Group. Intravenous ketogenic diet therapy for treatment of acute stage of super-refractory status epilepticus in a pediatric patient. Pediatr Neurol 2015; 52: 442-445.
- 3. Lin KL\*, Lin JJ, Hsia SH, Chou ML, Hung PC, Wang HS; CHEESE Study Group. Effect of antiepileptic drugs for acute and chronic seizures in children with encephalitis. PLoS One. 2015 Oct 7;10(10):e0139974.
- 4. Lin JJ1, Lin KL1,\*,, Wang Y, Wang HS, Hsia SH, Chang LY; CHEESE Study Group. CTLA-4+49 A/G polymorphism and antiglutamic acid decarboxylase antibody-associated encephalopathy in Taiwanese children. Brain Dev. 2015 Nov 3
- 5. Chiang MC, Lien R, Chu SM, Yang PH, Lin JJ, Hsu JF, Fu RH, Lin KL. Serum lactate, brain magnetic resonance imaging and outcome of neonatal hypoxic ischemic encephalopathy after therapeutic hypothermia. Pediatr Neonatol 2016 Feb;57(1):35-40.



## **Sunit SINGHI**

Professor and Head, Department Of Pediatrics, MM Institute of Medical Sciences And Research, Mullana- Ambala, India

Dr. Sunit Singhi is an acknowledged leader in Pediatric Critical Care and has contributed to development of the specialty globally. He is current President of World Federation of Pediatric Intensive and Critical Care Societies and was Vice President in 2012-13.



He started India's first fellowship programme in Ped Crit Care. An Associate Editor of Pediatric Critical Care Medicine, he is a fellow of National Academy of Medical Sciences and American College of Critical Care Medicine, Indian Academy of Pediatrics, Indian College of Critical Care, He has received "Plaque of Honor' from Brazilian Society for intensive care, Swasth Bharat Award for Pediatrics 2011, for contribution to public health care system in India, Amrut Mody Unichem Prize 2010 of Indian Council Of Medical Sciences for contributions to develop and conduct Pediatric Critical Care Courses all over the country and Life-Time Achievement Award of of Indian Society of Critical Care Medicine, and several medals, orations and best paper prizes. His paper on CNS infections received last year's BMJ Award in the category "Best Research Paper".

Prof. Singhi has made significant original contributions in the understanding of fluid, electrolytes and body water compartments, and treatment of bacterial meningitis, pneumonia, status epilepticus and acute severe asthma with help of more than a dozen research grants from WHO, ICMR, CCMRC, INCLEN and Sweden. He has more than 350 research papers in Indexed Journals, eleven books and 65 book chapters to his credit. He is currently engaged in collaborative research with Karolinska Institute, Stockholm, Sweden, on biomarkers in CNS infections in children.

# Tatsuya KAWASAKI

#### Present Position

Director of Pediatric Intensive Care Unit, Shizuoka Children's Hospital

#### Education

1999 MD, School of Medicine, the University of Tokyo

#### Academic Appointments

- 2000 Department of Pediatrics, Chiba-Nishi General Hospital
- 2002 Neonatal/Pediatric Intensive Care Unit, Nagano Children's Hospital
- 2004 Department of Anesthesiology, Saitama Children's Medical Center
- 2005 Department of Nephrology, Shizuoka Children's Hospital
- 2006 Paediatric Intensive Care Unit, Royal Children's Hospital, Melbourne
- 2008 Intensive Care Unit, Alfred Hospital, Melbourne
- 2009 Department of Pediatric Critical Care, Shizuoka Children's Hospital
- 2015 Director of Pediatric Intensive Care Unit, Shizuoka Children's Hospital



## **George IMATAKA**

#### Education

- 2012-2016: Dokkyo Medical University School of Medicine, Graduate School of Medicine (Ph.D., Pediatric Neurology)
- 2015- : London School of Marketing, Hon Kong, in Business Management
- 2011- : Keio University, correspondence course (Bachelor of Laws, LL.B.)

2008-2011 : Keio University (Bachelor of Philosophy, B.Phil.)

- 2005 : Dokkyo Medical University School of Medicine (Ph.D., Pathology)
- 1988-1994 : Dokkyo Medical University School of Medicine (M.D.)

### Present Appointment

- 2014- : Associate Professor, Department of Pediatrics, Dokkyo Medical University School of Medicine
- 2014- : Lieutenant Colonel (LTC) Japan Ground Self-Defense Force, (Reserve)
- 2009-2014 : Lecture, Department of Pediatrics, Dokkyo Medical University School of Medicine

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# Hiroshi ARAI

#### Present position

Chief, Department of Pediatric Neurology, Morinomiya Hospital (Osaka, Japan) Vice Director, Bobath Memorial Hospital (Osaka, Japan)

## Academic Appointment

Chair, Committee of Challenged Children, Osaka Pediatric Association

Member, Pediatric Medicine Committee, Japan Pediatric Society

### Biography

- 1987 Department of Pediatrics, Osaka University Hospital (Resident)
- 1997 Department of Pathology, Osaka Medical Center and Research Institute for Maternal and Child Health
- 1998 Department of Pediatric Neurology, Bobath Memorial Hospital (Chief)
- 2006 Department of Pediatric Neurology, Morinomiya Hospital (Chief)
- 2016 Bobath Memorial Hospital (Vice Director, concurrent)


# ABSTRACTS

**Invited Lectures** 

## L-01

## **OVERVIEW OF ISAE2016**

#### Hideo YAMANOUCHI

Department of Pediatrics, Saitama Medical University

As an introduction to the International Symposium on Acute Encephalopathy in Infancy and Its Related Disorders (ISAE2016), I would like to explain how this symposium came about. While we have been actively engaging in discussions and debates regarding acute encephalopathy and encephalitis in infancy and childhood in each country, there has been little opportunity to have discussions and collaborations worldwide with respect to these fields. When we are operating independently of each other, it is hard to align understanding of pathophysiology, to make precise and prompt diagnosis, and to optimize case management, therefore limiting our overall results. However, if we work together to solve these difficult problems, the opportunity for the evolution of progress will naturally follow. Hence, my motivation to hold this symposium was stimulated by this lack of sharing of ideas within the international community.

This symposium is comprised of three principal sections; Day 1, discussions on basic mechanisms to develop pathophysiology; Day 2, diagnoses of types of acute encephalopathy and encephalitis; Day 3, opinion exchanges about case management, including therapeutic hypothermia and status epilepticus as well as intractable epilepsy as neurological sequelae. I sincerely hope that this symposium will be a first step to start worldwide study on three principal pillars of acute encephalopathy and encephalitis in infancy.

## DEFINITION, CLASSIFICATION AND EPIDEMIOLOGY OF ACUTE ENCEPHALOPATHY

#### Masashi MIZUGUCHI, Ai HOSHINO, Makiko SAITOH

Department of Developmental Medical Sciences, The University of Tokyo, Tokyo, Japan

Acute encephalopathy (AE) is clinically defined as severe and prolonged disturbance of consciousness of acute onset, often accompanied by seizures and signs of raised intracranial pressure. AE is preceded by a febrile infectious disease. The pathological substrate of AE is diffuse or widespread, non-inflammatory brain edema, which is visualized by neuroradiologic studies, such as CT and MRI. AE is classified in two ways. One is based on the pathogen of antecedent infection, and another on the clinico-pathological features of encephalopathy. For the latter classification, various syndromes, such as Reve syndrome (RS), acute necrotizing encephalopathy (ANE), acute encephalopathy with biphasic seizures and late reduced diffusion (AESD), and clinically mild encephalitis with a reversible splenial lesion (MERS), have been described and characterized. Despite a rare disorder, AE accounts for substantial mortality and morbidity of children, especially in East Asia. An epidemiologic study showed that AE affects hundreds of Japanese children every year. The most common pathogen is influenza virus (27%), followed by HHV-6 (17%) and rotavirus (4%). The most prevalent syndrome is AESD (29%), followed by MERS (16%) and ANE (4%). The overall mortality of AE has recently declined from 30% (late 1990s) to 6% (2010). 36% of patients are left with neurologic sequelae, such as intellectual and motor disabilities and intractable epilepsy.

L-02

## L-03 INSIGHTS INTO SEIZURES AND EPILEPSIES IN THE DEVELOPING BRAIN: TRANSLATIONAL STUDIES

#### Solomon L. MOSHÉ

Saul R. Korey Department of Neurology, Dominick P. Purpura Department Neuroscience and Department of Pediatrics, Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, New York, USA

While it is well understood that the developing brain is not a miniature version of the adult brain there is less attention given to specific windows of development that may mediate different effects on seizures and epilepsy as a function of sex. Furthermore, it is pertinent to identify how specific etiologies may induce seizures, determine the circumstances that epileptogenesis may proceed, and the factors that will be responsible for the occurrence of intractable epilepsies and associated comorbidities. The International League Against Epilepsy is developing a classification of seizures and epilepsies that can be used by researchers to develop models that have translational value for specific syndromes. To this goal, there is a need to reframe the questions asked to account for the variability of outcomes. The identification of common mechanisms allows the development of common therapeutic strategies to treat seizures, but not necessarily with the same effectiveness during development. There is increasing knowledge of new specific etiologies (ie genetics, inflammation, newly identified infections) that have a key role in epileptogenesis as well as an awareness that a combination of etiologies that may be present at discreet developmental windows require unique age and sex specific approaches. Understanding the key features and possible biomarkers that may allow for the expression of seizures/ epileptogenesis as it relates to etiology as well as the consequences taking into account maturational patterns of the brain (and may be in the future of systemic factors) and gender difference will provide new insights into creating therapeutic approaches leading to individualized treatments and precision based medicine.

### NEUROVIRULENCE OF HUMAN HERPESVIRUS 6B (HHV-6B): ENCEPHALITIS AND MESIAL TEMPORAL LOBE EPILEPSY

#### Tetsushi YOSHIKAWA

Department of Pediatrics, Fujita Health University, Toyoake, Japan

Primary HHV-6B infection can cause exanthem subitum, which is common febrile exanthematous illness in infants and young children. Clinical course of the disease is considered to be benign and self-limiting. However, central nervous system (CNS) complications have been demonstrated to be the most common complications of the disease. In some of the HHV-6B encephalitis patients, small amounts of viral DNA was detected in cerebrospinal fluid (CSF). In contrast to HHV-6B encephalitis at the time of primary viral infection, remarkably high copies of viral DNA was detected in CSF collected from the post-transplant HHV-6B encephalitis patients caused by viral reactivation. Thus, pathogenesis of HHV-6B encephalitis may be different between the patients with primary viral infection and those with viral reactivation after transplant. In addition to the encephalitis, recent studies have suggested that HHV-6B may play important role in pathogenesis of mesial temporal lobe epilepsy (MTLE), which is one of the most common and intractable forms of seizure disorders. The most common pathological finding of MTLE is mesial temporal sclerosis (MTS) characterized by atrophy of brain tissues with extensive astrogliosis and neuronal loss in the lesion. Recent our study also demonstrated that detection of HHV-6 DNA was higher in MTS patients than non-MTS patients. Although no HHV-6B mRNA were detected in all samples, in MTS patients, expression of monocyte chemotactic protein-1 and glial fibrillary acidic protein were significantly higher in the amygdala samples with HHV-6 DNA than those without viral DNA.

L-04

## L-05 ICTOGENIC AND EPILEPTOGENIC MECHANISMS OF NEUROINFLAMMATION: INSIGHTS FROM ANIMAL MODELS

Annamaria VEZZANI, Valentina Iori, Federica Frigerio, Rosaria Pascente, Alberto Pauletti, Gaetano Terrone and Teresa Ravizza

Department of Neuroscience, IRCCS-Istituto di Ricerche Farmacologiche Mario Negri, Milano, Italy

The search of targets for developing novel drugs which can control drug-resistant seizures, or may prevent epilepsy development after potential epileptogenic insults in children and adults represents a great challenge for basic science. The available experimental and clinical evidence suggest that brain (neuro)inflammation due to the activation of the innate immunity system is both a contributing factor and a consequence of seizures. Emerging evidence pointed out to the crucial role played by glial cells, the innate immunity brain resident cells, in the generation of hyperexcitable neuronal networks underlying seizure generation and recurrence, as well as cell loss and comorbidities. Molecular and pharmacological studies targeting glia, and the inflammatory mediators released by these cells, in experimental models of pediatric and adult epilepsy highlighted novel targets for drug intervention aimed at interfering with disease mechanisms. The novel concept is that the inflammatory molecules released by parenchymal brain cells in diseased tissue have CNS-specific roles and mechanisms of action independent of their role in the classical immune/inflammatory responses occurring during infections. Insights into the mechanisms by which inflammatory molecules contribute to epileptogenesis and to seizure generation have highlighted either direct effects on neuronal function, or indirect effects mediated by alterations of endothelial and astrocytic cells physiology. In fact, some inflammatory molecules by activating their cognate receptors expressed by neurons directly increase neuronal excitability by modulating voltage-gated and receptor-operated ion channels. Among the indirect effects of inflammatory molecules on neuronal excitability, a prominent role has their ability to compromise the BBB permeability properties and the astrocyte-mediated buffering of extracellular K<sup>+</sup> and water homeostasis. Since activation of immunity and inflammation are endogenous homeostatic mechanisms, the challenge is to understand which inflammatory cells and related molecules can compromise brain physiology and promote seizures and neuropathology. In this context, the development of anti-inflammatory drugs interfering with the specific inflammatory signaling underlying ictogenesis and epileptogenesis might represent a promising therapeutic approach for inhibiting drug-resistant seizures, or for preventing the development of epilepsy and comorbidities in individual at risk.

### GENETIC BACKGROUND OF ENCEPHALOPATHY

#### Shinichi HIROSE

Department of Pediatrics, School of Medicine and Central Research Institute for the Pathomechanisms of Epilepsy, Fukuoka University, Fukuoka Japan

The molecular pathomechanisms of acute encephalopathy (AE) remain largely unknown. The high incidence of AE in the East Asian ethnicity suggests its underlying genetic background. AE, however, consists of multiple disorders and hence its heterogeneity as well as its rarity hider molecular genetic analyses. Nevertheless, several studies including ours have been implemented to identify the genetic background of AE. The neuroinflammatrory aspect of AE became a clue to identify the association of specific HLA class II types in susceptibility to acute necrotizing encephalopathy (ANE) and a mutation of the Toll-like receptor 3 gene in influenza-associated encephalopathy. A positional cloning approach identified a mutation of RANBP2, the gene encoding the nuclear protein Ran binding protein 2 in familial acute necrotizing encephalopathy (ANE). To the present, a numbers of *RANB2* mutations have been found and evidence that genetic factors contribute to the pathogenesis AE. The following studies were conducted mainly using the candidate gene approach and have identified polymorphisms and mutations in several genes, which predispose children to AE. Thus, polymorphisms in the genes encoding carnitine palmitoyl transferase II (CPTII) and the adenosine A2A receptor (ADORA2A) were found to be associated with ANE and AE with biphasic seizures and late reduced diffusion (AESD). These findings imply that metabolic disturbances underlie AE. Mutations of the genes encoding  $Na^+$  channels (SCN1A and SCN2A) have been also identified in AE. Since these mutations are known as the causes of fever sensitive epileptic encephalopathies such as Dravet syndrome, the findings suggest a close link between AE and such genetic epilepsies. These genetic identifiers and future massive genetic analyses on larger cohorts of AE using next generation sequencing should provide new insights on the genetic background of AE. The understanding of AE at molecular basis should shed lights on developing both therapeutic and preventive measures for AE.

L-06

## L-07 NEUROINFLAMMATION IN THE PATHOGENESIS OF EARLY LIFE EPILEPTIC ENCEPHALOPATHIES

#### Aristea S. GALANOPOULOU

Albert Einstein College of Medicine, Bronx, NY, USA

- <sup>1)</sup> Saul R. Korey Department of Neurology, Albert Einstein College of Medicine, Bronx, NY, USA
- <sup>2)</sup> Dominick P. Purpura Department of Neurology, Albert Einstein College of Medicine, Bronx, NY, USA
- <sup>3)</sup> Laboratory of Developmental Epilepsy, Albert Einstein College of Medicine, Bronx, NY, USA
- <sup>4)</sup> Montefiore / Einstein Epilepsy Center, Montefiore Medical Center, Bronx, NY, USA

Early life epileptic encephalopathies are a heterogenous group of disorders that have profound impact on the neurodevelopment of infants and children due to the difficult to treat seizures and epileptic activities and the disruption of processes that are important for the cognitive and behavioral development. Multiple etiologies, genetic or acquired, have been implicated in their pathogenesis. Recently, a growing list of pertinent animal models have been developed and offered insight into the pathogenesis and treatments of early life epileptic encephalopathies.

The contribution of neuroinflammatory pathways in the pathogenesis of epileptic seizures and the comorbidities of early life epileptic encephalopathies have been investigated in both clinical and animal studies. In human studies, there is evidence for abnormal expression of inflammatory cytokines in infants with epileptic encephalopathies with infantile spasms (West syndrome). Genetic studies in individuals with West syndrome or Lennox Gastaut syndrome have implicated several affected genes that mediate the effects of inflammatory pathways.

To determine whether neuroinflammation causes epileptic encephalopathies, we have used rodent models of infantile spasms induced through a variety of methods. We have compared the established multiple-hit rat model of infantile spasms due to structural lesions with novel models induced exclusively with pro-inflammatory compounds. Our findings indicate that neuroinflammation can indeed induce epileptic spasms and interictal epileptic activity in an age-specific manner. Novel treatments targeting the activated inflammatory pathways can suppress spasms. Longer-term outcomes are however modified by concomitant structural lesions, other molecular defects, or other underlying pathologies.

### **NEUROIMAGING IN ACUTE ENCEPHALOPATHY IN JAPAN**

#### Jun-ichi TAKANASHI

Department of Pediatrics, Yachiyo Medical Center, Yachiyo, Japan

The pathologic substrate of acute encephalopathy is diffuse or widespread, noninflammatory brain edema. In Japan, acute encephalopathy is usually preceded by infection, most often by influenza virus or human herpes virus (HHV) 6 and 7, and its incidence is highest in infancy and early childhood. Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) and clinically mild encephalitis/ encephalopathy with a reversible splenial lesion (MERS) are the most common subtypes of encephalopathy in Japan, in which MRI is the key for the diagnosis.

AESD is characterized clinically and radiologically by,

- 1. Febrile seizures as initial symptom within 24 hours of the onset of fever, most often lasting longer than 30 minutes.
- 2. Improvement of consciousness levels after the initial seizure, some with clear consciousness, sometimes leading to misdiagnosis of FS status.
- 3. Subsequent seizures, most often in cluster of CPS, between 4 and 6 days.
- 4. Outcome ranging from almost normal to severe mental retardation.
- 5. Reported only from Japan (or East Asian).
- 6. Within day 2, normal MRI.
- 7. Days 3 to 9, subcortical reduced diffusion, U-fiber lesion on T2WI, predominantly frontal or frontoparietal with sparing of perirolandic region.
- 8. After 2 weeks, cerebral atrophy.
- 9. Excitotoxic injury (elevated glutamate/glutamine on MR spectroscopy) with delayed (or apoptotic) neuronal death being hypothesized as a possible mechanism. MERS is characterized clinically and radiologically by,
- 1. Relatively mild clinical courses, and clinically recovered completely within a month (most often within a week) after the onset of neurological symptoms.
- 2. Homogenously reduced diffusion of the corpus callosum at least involving splenium (type 1), occationally, accompanying lesions in the symmetrical subcortical white matter predominantly in the peri-Rolandic region with the same signal character (type 2).
- 3. Hyponatremia due to SIADH is common.

## L-09 ELECTROENCEPHALOGRAPHY IN CHILDREN WITH ACUTE ENCEPHALOPATHY

### <u>Akihisa OKUMURA</u>

Department of Pediatrics, Aichi Medical University, Nagakute, Japan

Electroencephalography (EEG) is useful to evaluate brain function in children with impaired consciousness. However, its usefulness in acute encephalopathy has not been fully elucidated. I will present EEG and amplitude-integrated EEG (aEEG) findings and discuss their usefulness in children with acute encephalopathy.

1) EEG findings of children with acute encephalopathy

The most well-known EEG findings in acute encephalopathy is generalized slowing. However, EEG of children with acute encephalopathy may reveal some different findings such as focal slowing, low voltage background, absence of fast waves/ spindles, and excessive fast waves. In our experience, generalized or focal slowing was common in children with MERS, and absence of fast waves/ spindles was frequent in children with AESD. This suggest that EEG abnormalities can be different according to the subtype of acute encephalopathy.

2) Differentiation between acute encephalopathy and prolonged febrile seizures (FS).

One of the challenge regarding acute encephalopathy will be an early differentiation between acute encephalopathy and prolonged FS, because a long seizure is very frequent as an initial symptom of acute encephalopathy, especially of AESD. Several trials such as a scoring for early diagnosis have been made. We compared EEG in the first few days after seizure between AESD and prolonged FS, and found that absence of fast waves/spindles was more frequent in AESD than in prolonged FS. This indicates the usefulness of EEG in early diagnosis of acute encephalopathy.

3) aEEG monitoring in children with acute encephalopathy.

aEEG is a time-compressed trendgram of EEG. aEEG has been proven to be useful for seizure monitoring in neonates. aEEG can be applied for monitoring of brain function and seizures also in children with acute encephalopathy. Our previous studies showed clustering seizures without clinical symptoms in some children with acute encephalopathy. The efficacy of antiepileptic drugs can be evaluated objectively using aEEG.

## EEG FINDINGS DURING ACUTE PHASE OF PROLONGED FEBRILE L-10

#### Sooyoung LEE

Department of Critical Care Medicine, Fukuoka Children's Hospital, Fukuoka , Japan

It is difficult to identify pediatric acute encephalopathy (AE) and prolonged febrile seizure (PFS) in acute phase. Both of them manifest the same neurological symptoms of status epilepticus and impaired consciousness, with mimicking EEG pattern.

The sequential EEGs of PFS show diffuse high voltage slowing during first 2 hours after termination of seizure that gradually improved within 2~6 hours and become normal sleep pattern or continuous low~moderate amplitude  $\theta \sim \alpha$  activity. Anticonvulsant use may not change the course. To distinguish AE and PFS in acute phase, we recruited 40 children with AE (acute encephalopathy with biphasic seizures and late reduced diffusion (AESD)=4, Hemorrhage shock and encephalopathy syndrome (HSES)=2 ,Clinically mild encephalitis/encephalopathy with reversible splenial lesions (MERS)=3) and PFS (n=31) within 6 hours of presentation. The sequential EEGs of AESD show the same pattern. Some MERS shows occipital/frontal rhythmic slow wave burst. The EEGs of HSES show electrical storms and generalized periodic discharges (GPDs). It is difficult to distinguish some type of AE (AESD,MERS) and PFS.

GPDs, electrical storm, low amplitude low activity pattern and burst suppression pattern are seen in severe cases of AE, but not in patients with PFS .Quantitative EEG using fast Fourier transform reveals the tendency of acute phase sequential change of PFS patient's EEG. This tendency may help to distinguish AE and PFS.

## L-11 ACUTE ENCEPHALOPATHY WITH FEBRILE CONVULSIVE STATUS(AEFCSE/ AESD) and HHE SYNDROME : ACUTE BRAIN DAMAGE PROVOKED BY FEBRILE STATUS EPILEPTICUS

Masashi SHIOMI

Department of Pediatrics, Aizenbashi Hospital, Osaka, Japan Department of Pediatric Emergency Medicine(before 2011), Osaka, Japan

Acute encephalopathies (AE) associated with viral disease, such as influenza and HHV6, are serious diseases with mortality and morbidity in Japan. After mandatary influenza vaccination for schoolchildren was repealed in mid-1990s, outbreaks of influenza encephalopathy (IE) became important public health problems. As an emergency pediatrician, I tried to classify IE neuroradiologically and proposed "acute encephalopathy with febrile convulsive status epilepticus, AEFCSE" as a new entity of AE in 2000. AEFCSE were accepted widely. AEFCSE is characterized by, sequentially, febrile convulsive status epilepticus (early seizure, ES), transient incomplete recovery of 2-4 days duration, then reiterated afebrile focal convulsions (late seizure, LS) for a week with neurological deterioration, and sequelae. In LS phase, CT shows localized cerebral edema, named as "lobar edema, LE". MRI-DWI shows high signals in subcortical white matter of affected lobes, named "bright tree appearance, BTA", developed on 3-9 days of illness and disappeared thereafter. Takanashi described this disease as acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) in 2006. The hemispheric type of AEFCSE is identical to "idiopathic" hemiconvulsion-hemiplegia syndrome. But a distribution of LE/BTA is various in combination, such as bi-frontal, hemi-temporal, etc in AEFCSE. The common age of AEFCSE is one year, compatible with that of febrile seizure. In AEFCSE theophylline had been a precipitating factor before 2005 when theophylline was withdrawed in infants. According to Mizuguchi's national survey of AE, AESD/AEFCSE was the most frequent syndrome in AE and the estimated number of annual cases was ca.200. Because differentiation from febrile seizure is difficult in ES phase, the results of several clinical trials to treat AEFCSE are indefinite or ineffective. But targeted temperature management after ES may be promising. I suppose the early use of im midazolam for febrile seizure in prehospital settings will be reduce AEFCSE, like AED for cardiac arrest.

## ACUTE NECROTIZING ENCEPHALOPATHY: CLINICAL, PATHOLOGIC AND GENETIC STUDIES

L-12

#### Masashi MIZUGUCHI, Ai HOSHINO, Makiko SAITOH

Department of Developmental Medical Sciences, The University of Tokyo, Tokyo, Japan

Acute necrotizing encephalopathy (ANE) is a fulminant type of acute encephalopathy most prevalent in East Asia. ANE is most common in infants and young children under 5 years of age, but is occasionally seen in adults. The most common pathogen of antecedent infection is influenza virus, followed by HHV-6. ANE is a systemic disorder presenting with both the brain dysfunction (rapidly progressive coma, convulsion, signs of raised intracranial pressure) and systemic organ disorders (liver dysfunction, hopotension, DIC, hemophagocytic syndrome). The diagnosis of ANE is based on the characteristic CT/MRI findings: multiple, symmetric lesions in the bilateral thalami and other brain regions, such as the putamina, cerebral and cerebellar deep white matter, and brainstem tegmentum. Pathological studies of these brain lesions demonstrate severe damage to cerebral blood vessels. The center of thalamic lesions shows capillary hemorrhage and necrosis, while the periphery shows edema with perivascular leakage of plasma. There is no infiltration of inflammatory cells, except for activation of microglial cells. Despite the efficacy of corticosteroid therapy, the prognosis of ANE remains poor. About 30% of patients die, and 60% are left with neurologic sequelae. The etiology of ANE is most likely multi-factorial. Genetic studies have identified several risk genotypes, such as specific HLA types and cytokine gene polymorphisms.

Several conditions, such as familial, recurrent ANE (ANE1) and acute encephalopathy complicating enterohemorrhagic *E. coli* infection, also show symmetric brain lesions similar to those of ANE. Despite many differences in epidemiologic, clinical and radiologic features, they may be regarded as variants of ANE.

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## L-13

## ACUTE NECROTIZING ENCEPHALOPATHY IN TAIWAN AND GLOBAL STUDY ON ACUTE ENCEPHALOPATHY

I-Jun CHOU<sup>1)</sup>, Huei-Shyong WANG<sup>1)</sup>, Kuang-Lin LIN<sup>1)</sup>, Alex M WONG<sup>2)</sup>

Acute necrotizing encephalopathy (ANE) is a hyperacute catastrophic neurological condition presented with rapidly deterioration of consciousness and cascade changes involving thalami, periventricular white matter, internal capsule, putamen, brainstem, and cerebellum. It was commonly isolated event, while cases with recurrent disease and familial aggregation have been reported. Genetic susceptibility probably is the foundation of pathogenesis. Patients are mostly infants and young children, although adult cases were occasionally reported.

Patients with ANE in Taiwan have been reported in children aged 2 months to 12 years old. Familial cases had been identified recently. After 1-3 days of fever, coma with magnetic resonance (MR) evidence of T2-hyperintensed thalami is cardinal finding, which may accompany with acute/subacute hemorrhage and evolve to cavitation during follow-up. Rarely, it can involve the spinal cord. Several viruses especially influenza were identified in these patients, however pathogens were not identified in some patients despite extensive evaluation. Outcomes of these patients were variable and MR imaging score, which composites of presence of hemorrhage, cavitation, and location of lesions, can help predict outcome. The brain stem involvement can be fatal and lead to poor outcome.

ANE has been reported worldwide. However, familial or recurrent cases were more commonly in countries outside Asia and sporadic cases were generally more common in Asian countries. Culprit gene in recurrent familial cases reported in the United states by Neilson et al. in 2003 was autosomal dominant with incomplete penetration (RANBP2 gene at 2q13). This gene accounts for most familial or recurrent cases, however other unidentified genetic loci are possible. The features between sporadic cases and familial cases were intriguingly similar although Neilson et al. proposed patients with RANBP2 mutations have involvement of the external capsule, extreme capsule, claustrum, medial temporal lobes, amygdale, hippocampi, and spinal cord in addition to the typically affected areas of the brain.

<sup>&</sup>lt;sup>1)</sup> Department of Pediatrics, Division of Pediatric Neurology, Chang Gung Children's Hospital and Chang Gung University, Kwei-Shan, Tao Yuan, Taiwan

<sup>&</sup>lt;sup>2)</sup> Department of Medical Imaging and Intervention, Chang Gung Memorial Hospital and Chang Gung University, Kwei-Shan, Tao Yuan, Taiwan

### ACUTE ENCEPHALOPATHY AS AN INITIAL MANIFESTATION OF MITOCHONDRIAL DIEASES AND RELATED DISORDERS

L-14

#### Hitoshi OSAKA

Department of Pediatrics, Jichi Medical University, Shimotsuke, Japan

Mitochondrial disease can manifest as acute encephalopathy triggered by febrile illnesses, which increase energy demand and reveals the underlying failure of the respiratory chain to produce adenosine triphosphate (ATP). Metabolic decompensation also occurs in other inherited metabolic diseases, such as amino acid, organic acid, carbohydrate, and b-oxidation deficits. Two subgroups of mitochondrial diseases are important: Leigh syndrome/encephalopathy (LS) and mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome.

In LS, energy failure damages a subset of neuronal cells with a high ATP requirement; this damage results in brainstem and basal ganglia lesions similar to those observed in anoxic encephalopathy. Cellular dysfunction near the reticular formation in the brainstem distorts consciousness. Clinically, brain stem lesion causes symptoms such as nystagmus and swallowing difficulty. Basal ganglia lesion may cause rigidity and dystonia. These lesions can be visualized using brain magnetic resonance imaging. Magnetic resonance spectroscopy can be used to reveal elevated lactic acid, a hallmark of LS. As the oxidation-reduction potential is affected by respiratory chain defects, the lactate values are disproportionately elevated and the lactate/pyruvate ratio is increased more than 20-fold. Chronically insufficient ATP supply in the central nervous system typically causes a developmental delay before episodes of encephalopathy emerge. More than 100 nuclear and mitochondrial genes are responsible for LS.

In MELAS syndrome, insufficient blood supply to the cerebrum produces stroke-like episodes. Cellular malfunction in the unilateral cerebrum can disturb consciousness and mimic acute encephalopathy. Careful family history taking would reveal deafness, diabetes, etc. in maternal relatives. Short statue, hirsutism, and easy fatigability are the key to diagnosis. More than 80% of MELAS cases have a common mutation, m.3243A>G, in the mitochondrial tRNA<sup>Leu(UUR)</sup> gene.

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## L-15 ENCEPHALITIS/ENCEPHALOPATHY AND NEURODEVELOPMENTAL DISORDERS

#### Yushiro YAMASHITA

Department of Pediatrics & Child Health, Kurume University School of Medicine, Kurume, Japan

Encephalitis/encephalopathy in children can lead to significant long-term neurological sequelae. Severe neurologic disabilities, such as motor deficits, mental retardation, and intractable seizures are common. Among survivors who had fully recovered, reduced neurocognitive performance, behavioral, and learning problems can happen.

In this luncheon seminar, I will mainly focus on attention deficit hyperactivity disorder (ADHD) associated with encephalitis/encephalopathy. ADHD is a neuro-developmental disorder with an estimated prevalence among children and adolescents of 5%. It is highly heritable disorder, but childhood illness such as viral meningitis and encephalitis/ encephalopathy were associated with ADHD. Viral infections during pregnancy had an increased risk of ADHD. Other viral infections associated with increased prevalence of ADHD included enterovirus 71, HIV, HSV, and influenza virus. Fowler reported that as many as 54% of Swedish children with acute encephalitis (n=71) had persistent symptoms at long-term follow-up evaluations. Micheaeli et al. revealed Islaeli children (n=47) with encephalitis had a significantly higher prevalence of ADHD (50%) and learning disabilities (20%) compared with the reported rate (5-10%) in the general population. Kurihara investigated the prognosis of 103 Japanese children with acute encephalopathy at more then one year from the onset. Complicating disabilities comprised mental retardation (89.3%), higher cortical dysfunction (77.7%), epilepsies (68.9%), and motor disturbance (27.2%). Attention deficit and visiospacial disturbance were the main symptoms of higher cortical dysfunction.

Further studies for the analysis of determinants of outcomes; e.g. impact of certain treatments (cooling following acute child encephalitis/encephalopathy), long-term neurocognitive follow-up, and the development of effective intervention to reduce the disabilities after encephalitis/encephalopathy are necessary.

### GENETIC-METABOLIC DISORDERS PRESENTING AS ACUTE, BUT REVERSIBLE, SEVERE EPILEPSIES

L-16

#### Phillip L. PEARL

Department of Neurology, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA

Multiple genetic-metabolic epilepsies are amenable to treatment that markedly improves the disease course. Knowledge of these amenably treatable severe pediatric epilepsies allows for early identification, testing and treatment. These disorders present with various phenotypes, including early onset epileptic encephalopathy (including refractory neonatal seizures, early myoclonic encephalopathy, and early infantile epileptic encephalopathy), infantile spasms, or mixed generalized seizure types in infancy, childhood, or even adolescence and adulthood. A typical clinical presentation is that of a newborn with impaired feeding who is noted to ultimately become encephalopathic with hypotonia, lethargy, or respiratory distress. Myoclonic seizures are classic, although apneic episodes, oculofacial movements, grunting, and epileptic spasms are also well described ictal events. EEGs may show discontinuous patterns characterized by burst-suppression, continuous or frequent intermittent generalized sharp or spike-wave activity, hypsarrhythmia, or multifocal spike discharges superimposed upon background disorganization including loss of normal sleep architecture. The clinical task of identifying these disorders is made more complicated, however, by nonspecific presentations that include failure-tothrive, developmental delay, or recurrent vomiting, and by varying presentations of the same disorder. The disorders are presented as vitamin responsive epilepsies including pyridoxine, pyridoxal-5-phosphate, folinic acid, and biotin; transportopathies including GLUT-1, cerebral folate deficiency, and biotin thiamine responsive disorder; amino and organic acidopathies including serine synthesis defects, creatine synthesis disorders, molybdenum cofactor deficiency, cobalamin deficiencies; mitochondrial disorders; urea cycle disorders; neurotransmitter defects including biopterin synthesis/recycling defects; and disorders of glucose homeostasis with neonatal diabetes or congenital hyperinsulinism. In each case, targeted intervention directed toward the underlying metabolic pathophysiology affords for the opportunity to significantly impact the outcome and prognosis of an otherwise severe pediatric epilepsy.

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## L-17 ACUTE ENCEPHALOPATHY IN INFANTS WITH SULFITE OXIDASE AND MOLYBDENUM COFACTOR DEFICIENCY

Hsiu-Fen LEE<sup>1)</sup>, and Ching-Shiang CHI<sup>2)</sup>

<sup>1)</sup> Department of Pediatrics, Taichung Veterans General Hospital, Taichung, Taiwan

<sup>2)</sup> Department of Pediatrics, Tungs' Taichung Metroharbor Hospital, Taichung, Taiwan

Sulfite oxidase is a mitochondrial enzyme that oxidizes potentially toxic sulfites to nontoxic sulfates. It is one of three enzymes that require molybdenum as a cofactor, the other two being xanthine oxidase and aldehyde oxidase. Reduced activity of this enzyme either results from an isolated deficiency of the enzyme itself or is secondary to deficiency of the cofactor molybdenum.

Both isolated sulfite oxidase deficiency and molybdenum cofactor deficiency are rare recessive inborn errors of metabolism, and the two diseases result in identical clinical features and radiological alternations. Presentations are usually in the neonatal period, including seizures, movement disorder, feeding difficulty, and irritability. The initial neuroimaging studies show diffuse cortical swelling or cystic cavities of the cerebral cortexes. Clinical features closely resemble those of hypoxic ischemic encephalopathy. During the period of follow-up, microcephaly, spastic paraplegia, myoclonus, and opisthotonus are common. Dysmorphic facial stigma can be similar to that in patients with perinatal asphyxia. Ocular abnormalities include lens dislocation, spherophakia, iris coloboma, nystagmus, and enophthalmos. Neuroimaging studies reveal a diffuse pattern of brain atrophy with arrested development of myelination, evidence of gliosis, and cystic necrosis of cerebral white matter, and dilated ventricles. Medical treatments in both diseases remain supportive except that molybdenum cofactor type A deficiency can be treated with cPMP.

It is imperative to differentiate from hypoxic ischemic encephalopathy, given its genetic implications.

L-18

## OVERVIEW OF CLINICAL RECOGNITION, AUTOANTIBODY DIAGNOSTIC MARKERS AND TREATMENT OF AUTOIMMUNE ENCEPHALITIS

#### Russell C. DALE

Institute for Neuroscience and Muscle Research, the Children's Hospital at Westmead, University of Sydney, Australia

Encephalitis is a complex syndrome, caused by 'inflammation of the brain' with heterogenous presentations and multiple causes. Encephalitis is a serious disease with ~5% mortality, and 50% of survivors have residual problems. Recent discoveries have defined a 'new' group of encephalitis which is associated with autoantibodies against cell surface neuronal antigens, which are typically neuronal receptors or synaptic proteins. These autoimmune encephalitis syndromes can be separated into autoimmune encephalitis and autoimmune demyelinating encephalomyelitis. The classic autoantibody associated with autoimmune encephalitis is anti-NMDA receptor antibody, and the most common autoantibody associated with autoimmune demyelination is anti-myelin oligodendrocyte glycoprotein (MOG) antibody. Anti-NMDAR encephalitis in its full form is very recognizable with psychosis, memory deficits, dyskinetic movement disorders, dysautonomia and seizures. Anti-MOG antibody associated disease includes acute disseminated encephalomyelitis, but also optic neuritis and transverse myelitis (but not multiple sclerosis). The treatment of these disorders generally involves broad spectrum immune suppression including corticosteroids, intravenous immunoglobulin and/ or plasma exchange, and if severe, rituximab or cyclophosphamide. Relapsing disease may require chronic immune suppression. A new development of great interest is the observation that confirmed herpes simplex virus encephalitis can induce a secondary autoimmune encephalitis with NMDAR antibodies, and this syndrome is also responsive to immune suppression. The study of CSF cytokines and chemokines have expanded our understanding of these disorders and improved our ability to monitor patients and define ongoing CNS inflammation. General themes in the treatment of autoimmune encephalitis include: 1. Early diagnosis and early treatment improves outcomes; 2. If a patient fails to respond to first line therapy, second line therapy (such as rituximab) should be considered.

## L-19 NATIONWIDE SURVEY OF ACUTE DESSEMINATED ENCEPHALOMYELITIS IN JAPAN

### Hiroyuki TORISU<sup>1,2)</sup>

<sup>1)</sup> Department of Pediatrics, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

<sup>2)</sup> Section of Pediatrics, Department of Medicine, Fukuoka Dental College, Fukuoka, Japan

**Objective:** To investigate the clinical and epidemiological features of pediatric cases of acute disseminated encephalomyelitis (ADEM) in Japan.

**Methods:** We conducted a nationwide survey of pediatric cases of acquired demyelinating syndromes of the central nervous system (ADS) and collected clinical data on children with ADS, including ADEM, aged less than 16 years who visited hospitals within the period from 2005 to 2007.

**Results:** Among the 977 hospitals enrolled, 723 (74.0%) responded to our inquiries and reported a total of 439 patients, including 244 with ADEM. We further collected and analyzed the detailed recorded data from 204 patients, including 66 with ADEM. The annual incidence rate of pediatric ADEM in Japan was estimated at 0.40 cases per 100,000 children (95% confidence interval, 0.34-0.46), and the incidence of ADEM in northern Japan tended to be lower than those in the central and southern regions (p =0.09). The patients with ADEM had the youngest mean age at onset (5.5 years) and the lowest female-to-male ratio (33.3%) among those with pediatric ADS. Of the patients with ADEM, 62% had a preceding infection and 18% received vaccination. Seizures, visual loss, and gait disturbances were observed in 32%, 11%, and 59% of patients, respectively. Pleocytosis, elevated IgG index, and presence of oligoclonal band were found in 85%, 36%, and 8% of the patients, respectively. The mean number of cerebral lesions was 6.3. Optic nerve, brainstem, and spinal lesions were observed in 6.5%, 29%, and 38% of the patients, respectively. Most of the patients were treated with immunosuppressive therapy, including high-dose methylprednisolone (85%) and intravenous immunoglobulin (15%). The incidence of sequelae was 17%, but the mean Expanded Disability Status Scale scores was 0.29.

**Conclusions:** This study elucidated the characteristic clinical features of pediatric ADEM in the Japanese population.

L-20

## EARLY CLINICAL DIAGNOSIS & EVIDENCE FOR TREATMENT IN IMMUNE-MEDIATED ENCEPHALITIS WITH ANTIBODIES TO NMDA-TYPE GLURS

#### Yukitoshi TAKAHASHI

National Epilepsy Center, Shizuoka Institute of Epilepsy and Neurological Disorder, NHO, 886 Urushiyama, Aoi-ward, Shizuoka, Japan

Acute immune-mediated encephalitis constitutes 21% of encephalitis, and acute encephalitis with antibodies to NMDA-type GluRs constitutes 4%. Other antibodies to neural molecules causally related with encephalitis include antibodies to LGI1, Caspr2, GABABR, AMPAR, NAE, etc.

Non-herpetic acute limbic encephalitis (NHALE) is characterized by onset symptom related with limbic system, better life prognosis, and amnestic sequelae. NMDAR-encephalitis is characterized by antibodies to NMDA-type GluRs by cell-based assay. In our laboratory, we recognized 70-80% of NHALE patients with had antibodies to NMDA-type GluRs by ELISA, and 24.2% of patients with antibodies to NMDA-type GluRs by ELISA were pediatric patients.

We hypothesized that antibodies to NMDA-type GluRs had been produced before onset of NHALE, and that from prodromal stage the antibodies might bring mild neuropsychiatric symptoms. In preceding stage, fever as preceding symptom was found in 135/207 patients. Aseptic meningitis was frequent in patients aged from 30-39 years. Comparing with data in 42 age-matched controls, decreased lymphocytes and platelets in blood of 42 NHALE patients at preceding stage were found. Comparing with data of 78 age-matched aseptic meningitis patients, decreased glucose and increased protein levels in CSF were found in 17 patients at preceding stage.

In 100 patients, death rate was 5%, and disability of ADL was observed in 27.4%, epileptic seizures in 21.1%, psychiatric disorder in 30.4%, cognitive disorder in 42.9%, memory disorder in 48.9%, motor dysfunction in 18.9%. Outcome was better significantly in patients with earlier introduction of methyl-prednisolone pulse therapy. Supplementary prednisolone treatment after pulse therapy and continuous infusion of midazolam at the earlier stage seem to be related with higher death rate.

## ENCEPHALITIS IN THE TROPICS

L-21

<u>Pratibha SINGHI</u>, Head, Department of Pediatrics, Chief-Pediatric Neurology and Neurodevelopment

Department of Pediatrics, Advanced Pediatrics Centre, Postgraduate Institute of Medical Education & Research, Chandigarh. India

Acute encephalitis is common in tropics and is associated with high mortality and morbidity. Etiologies of acute encephalitis in tropics are different from those in non-tropical countries because of differences in geographic environments and vectors, compounded by inadequate health care and sanitation facilities. Japanese encephalitis is endemic in Asia with almost 68,000 cases occurring annually. Cerebral malaria, acute bacterial meningoencephalitis, Dengue, scrub typhus, typhoid, rabies, leptospirosis, fungal and parasitic infections are some of the important causes of encephalitis in the tropics, in addition to Herpes, enteroviruses etc.

Because of overlapping clinical presentations, specific diagnosis may be clinically difficult. A syndromic approach with epidemiologic and clinical clues helps in narrowing the differential diagnosis. Acute encephalitis with systemic manifestations such as rash, thrombocytopenia, transaminitis, shock and haemorrhage is seen in dengue, scrub typhus, typhoid fever, leptospira, cerebral malaria, measles, and mumps; causes of encephalitis with isolated neurological manifestations include Japanese B encephalitis, herpes, West Nile virus, Nipah virus, enterovirus encephalitis, and acute bacterial meningoencephalitis. Neurocysticercosis, naegleria, acanthamoeba, toxoplasma, cryptococcus are rare but important causes.

MRI with advanced imaging techniques is very helpful in predicting aetiology in relevant clinical contexts. Bilateral thalamic, basal ganglia, and brainstem involvement is highly suggestive of Japanese encephalitis in an endemic area. Dengue encephalitis shows cerebral edema, scattered focal lesions, thalamic, midbrain and basal ganglia involvement. Rabies encephalitis typically involves dorsal brain stem, basal ganglia, hypothalamus, spinal grey matter with nerve root enhancement. Diagnosis is confirmed with CSF analysis, serological tests and molecular methods.

Management includes supportive measures and specific treatment when available preferably in an intensive care unit. Widespread immunization has decreased JE in certain countries. Emergence of novel pathogens, increasing international travel, change in climate, increasing virulence, resistance to existing drugs, spread to newer geographical areas and poor response to vaccines are major hurdles to overcome.

## CLUSTERING OF ACUTE FLACCID MYELITIS OF UNKNOWN ETIOLOGY IN JAPAN, AUTUMN 2015

L-2

<u>Pin Fee CHONG</u><sup>1)</sup>, Ryutaro KIRA<sup>1)</sup>, Harushi MORI<sup>2)</sup>, Akihisa OKUMURA<sup>3)</sup>, Sawa YASUMOTO<sup>4)</sup>, Hiroyuki TORISU<sup>5)</sup>, Hiroyuki SHIMIZU<sup>6)</sup>, Keiko TANAKA-TAYA<sup>7)</sup>

<sup>1)</sup> Department of Pediatric Neurology, Fukuoka Children's Hospital, Fukuoka, Japan

<sup>2)</sup> Department of Radiology, the University of Tokyo, Tokyo, Japan

<sup>3)</sup> Department of Pediatrics, Aichi Medical University, Aichi, Japan

<sup>4)</sup> Medical Education Center, Fukuoka University School of Medicine, Fukuoka, Japan

<sup>5)</sup> Section of Pediatrics, Department of Medicine, Fukuoka Dental College, Fukuoka, Japan

<sup>6)</sup> Department of Virology II, National Institute of Infectious Diseases, Tokyo, Japan

<sup>7)</sup> Infectious Disease Surveillance Center, National Institute of Infectious Diseases, Tokyo, Japan

**Objective:** Cases of acute flaccid paralysis (AFP) were reported throughout Japan in autumn 2015, with most of them presenting as myelitis of unknown origin. To clarify the clinical characteristics of acute flaccid myelitis (AFM) cases.

**Methods:** Case series of patients presented with AFP reported to National Institute of Infectious Diseases with symptom onset between August to December 2015. AFM was defined using radiological and cerebrospinal fluid findings according to the CSTE definition 2015. Clinical characteristics, radiological and neurophysiological findings of AFM were assessed by reviewing medical charts retrospectively.

**Results:** At February 2016, 82 cases of AFP were identified, with 46 met the case definition of AFM. Median age was 3 years, and a peak incidence was noticed in September. Symptoms preceded neurological symptoms included fever (n=40), and respiratory symptoms (n=37). Neurological deficits included flaccid limb weakness (monoplegia n=19, paraplegia n=18, triplegia n=3, quadriplegia n=6), cranial nerve dysfunction (n=4), and neurogenic bowel and bladder (n=11). 39 patients had cerebrospinal fluid pleocytosis, and 45 patients had longitudinal lesions of T2 hyperintensity of spinal gray matter on MRI. Abnormal findings were detected in 82% of motor nerve conduction study and 79% of F-wave study. Despite treatment received, 44 patients showed persistent limb weakness at follow-up. Pathogens were detected from only a few cases, consisted of enteroviruses, echovirus, and others.

**Conclusions:** The high incidence of myelitis reported during this period was concurrent with a national enterovirus D68 outbreak occurring from August through October 2015. AFM showed poor motor prognosis and a system of vigorous surveillance is needed.

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## L-23 ACUTE ENCEPHALOPATHY WITH INFLAMMATION-MEDIATED STATUS EPILEPTICUS

### Raman SANKAR

Department of Neurology and Pediatrics, David Geffen School of Medicine, the University of California

(Rima Nabbout)

(Department of Pediatric Neurology, Paris Descartes University, France)

## L-24

### LIGHT FIRES IN THE BRAIN: DOES NEUROINFLAMMATION TRIGGER REFRACTORY STATUS EPILEPTICUS?

### Hiroshi SAKUMA

Developmental Neuroimmunology Project, Department of Brain Development and Neural Regeneration, Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan

Febrile infection-related epilepsy syndrome (FIRES) is a severe seizure disorder that presents with intractable status epilepticus after a febrile illness. The pathogensis of FIRES is still unknown despite extensive genetic, metabolic, and virological studies. Although vicious cycle of inflammation and seizure activity is postulated to aggravate refractory status epilepticus, there had been no evidence to support this hypothesis. We recently demonstrated that pro-inflammatory cytokines and chemokines were highly elevated in the cerebrospinal fluid from patients with FIRES, suggesting that neuroinflammation play an important role in the development of this condition. It is likely that up-regulation of inflammatory mediators is just a trigger of the disease, and it needs to be clarified how inflammation alters neuronal function.

Increasing evidence suggests that neuroinflammation affects neuronal excitability. Neuroinflammation not only regulates the expression of ion channels and neurotransmitter receptors, but also participates in controlling synapse. Microglia, brain-resident immune cells, continuously survey synapses and also eliminate unnecessary ones. ATP is released from postsynaptic area upon glutamate induced neuronal excitation and promotes the extension of microglial processes through P2Y12 purinergic receptor. Inactive synapses are tagged by C3 complement factor and are engulfed by microglia via C3 receptor. These neuron-microglia interactions exemplify how immune system modulates neuronal activity. In the healthy brain, microglia fine-tune synapses by activity-dependent selection, which is orchestrated by the network of purinergic and complement systems. On the contrary, microglial dysfunction may have detrimental effects on neural activities in the inflamed brain and is possibly associated with inflammation-mediated refractory status epilepticus. These findings provide support for the novel treatment strategy to manipulate neuroinflammation and neuron-microglia interaction.

## L-25 FEBRILE INFECTION-RELATED EPILEPSY SYNDROME (FIRES): LONG-TERM NEUROLOGICAL FOLLOW-UP

Hsiu-Fen LEE<sup>1)</sup>, Ching-Shiang CHI<sup>2)</sup>

<sup>1)</sup> Department of Pediatrics, Taichung Veterans General Hospital, Taichung, Taiwan

<sup>2)</sup> Department of Pediatrics, Tungs' Taichung Metroharbor Hospital, Taichung, Taiwan

Febrile infection-related epilepsy syndrome (FIRES) is a catastrophic epileptic encephalopathy. Patients described in this entity share common clinical characteristics, including a febrile infection preceding the onset of the prolonged disease in previously healthy children. Although different pathogeneses, including an immunological source, a genetic predisposition, and an inflammatory-mediated process, have been hypothesized, the actual pathomechanism remains unknown.

The seizure types at the onset of the disease are mainly focal seizures with or without evolving to bilateral convulsive seizures. The focal seizures are often with facial myoclonia. EEG recordings show focal, multifocal, or generalized epileptiogenecity. The initial brain MRI findings are usually normal, but signal changes are detectable in some patients, predominantly in the temporal regions, the insula, the basal ganglia, and/ or the thalami. Clinical seizures of those patients would last for more than one month despite intensive treatment with multiple antiepileptic drugs, immunosuppressive agents, a ketogenic diet, and/or burst-suppression coma. FIRES patients are usually with a high mortality rate or severe neurological sequelae, i.e., intractable epilepsy and cognitive function decline.

The outcome of FIRES is devastating. More studies are needed for further understanding of the etiology and possible precipitating factors of this specific condition, as better delineation of the syndrome is the first step to more effective management of this distressing catastrophic epileptic syndrome.

## FEBRILE INFECTION RELATED SYNDROME (FIRES): CLINICAL EXPERIENCE IN ITALY

## L-26

### Nicola SPECCHIO

Department of Neuroscience, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy

Febrile infection related syndrome (FIRES) is a condition that affects previously healthy children who develop severe focal epilepsy after an acute or sub-acute febrile encephalopathy. This is a severe condition with motor and/or cognitive sequaela. Etiology is still unknown, while some hypothesis on possible inflammatory mechanisms has been pointed out. In this condition have been recognized an Acute phase and a chronic phase.

The acute phase is Encephalitis/encephalopathy period in which at least one of the following symptoms or signs was continuously present from the onset: seizures, fever, soporous state, confusion, or neurological deficits.

The chronic phase is defined as a state of enduring drug-resistant focal epilepsy.

During acute phase all patients presented with focal seizures, with an alternating prevalence of side. Loss of contact and/or staring associated with head and/or eyes deviation toward one side and automatisms; sometimes followed by secondary generalization was the most common semiology. Temporal and frontal lobe involvement was the most common, slowing background activity, focal or diffuse slow waves. Chronic epilepsy occurs soon after the cessation of the acute phase with progressive recovery of consciousness. Seizures semiology in the chronic phase is very similar to that present during the acute phase. Ictal EEGs confirms seizure onsets in the bilateral temporal areas.

Cognitive outcome is variable ranging from behavioral symptoms to severe cognitive deterioration (memory deficit and frontal functions). The etiology of FIRES is unknown. The lack of clear diagnostic procedures for FIRES makes difficult to assess the outcome and prognosis. We would like to develop, through the study of retrospective and prospective cases of FIRES, a diagnostic flow-chart for a better definition of the syndrome and a focused therapeutic approach.

## CURRENT MANAGEMENT OPTIONS IN STATUS EPILEPTICUS

#### J. Helen CROSS

L-27

UCL-Institute of Child Health, Great Ormond Street Hospital for Children, London, UK

Status epilepticus is by definition continuing seizure activity for a duration of 30 minutes or more. Treatment however is preferably initiated prior to this time, to raise the chances of cessation and prevent resultant morbidity. Treatment of prolonged acute convulsive seizures is consequently recommended at 5 minutes. Benzodiazepines remain the first line treatment in any situation; they are rapid acting, safe and are available through many routes. Evidence suggests however that more than two administered doses is associated with respiratory depression, and also with seizures lasting longer than 30 minutes, consequently no more than two doses should be administered prior to second line medication, Second line treatment has traditionally been phenytoin although evidence is now building for other medications available intravenously such as sodium valproate or levetiracetam. A move to anaesthetic and ICU should occur with EEG monitoring if second line medication fails. Key to optimal management of prolonged seizures and status epilepticus however is utilization of protocols. Many guidelines exist, outlining medications to be used and timings of such but these need to be adopted locally and at times on an individual basis, with individualized care plans, in order to ensure communication and optimal management. The sooner treatment is initiated, the more likely seizures are to stop.

## MULTIMODAL APPROACH, MONITORING AND MANAGEMENT FOR FEBRILE REFRACTORY STATUS EPILEPTICUS

L-28

Kuang-Lin LIN<sup>1)</sup>, Jainn-Jim LIN<sup>2)</sup>

- <sup>1)</sup> Division of Pediatric Neurology, Chang Gung Children's Hospital and Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Taoyuan, Taiwan
- <sup>2)</sup> Division of Pediatric Critical Care and Pediatric Neurocritical Care Center, Chang Gung Children's Hospital and Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Taoyuan, Taiwan

Refractory status epilepticus is a state of persistent seizures lasting more than 2 hours despite optimal treatment with antiepileptic drugs. It is a neurologic emergency and can cause severe neurologic sequelae, even death. There are various causes of pediatric refractory status epilepticus and most of them are febrile related in children. Viral encephalitis, autoimmune encephalitis and febrile infection related-epilepsy syndrome are all propose to etiology of febrile refractory status epilepticus. The continuous electroencephalographic (cEEG) monitoring has been emphasized to direct treatment in intensive care unit. However, the refractory status epilepticus treatment strategies vary substantially from one institution to another due to the lack of data to support one treatment over another. We will review the literature of multimodal approach, monitoring and management for febrile refractory status epilepticus and report our experience in this topic.

## THE DRUGS DON'T WORK – WHAT NEXT?

#### J. Helen CROSS

L-29

UCL-Institute of Child Health, Great Ormond Street Hospital for Children, London UK

The first line treatment on a diagnosis of epilepsy remains antiepileptic medication. The ILAE definition of drug resistance highlights a response to be that where there is a duration seizure free three times the previous seizure free duration. Drug resistant epilepsy may be defined as a failure of adequate trials of two tolerated and appropriately chosen and used AED schedules, whether as monotherapies or in combination, to achieve sustained seizure freedom. However when an individual presents with apparent drug resistance there needs to be an initial assessment that this is indeed the case- not least that the diagnosis is accurate. If true drug resistance is demonstrated consideration should be given as to whether surgical treatment may be an option, and referral made accordingly. Carefully selected children may benefit from focal resection where seizures are demonstrated to arise from a single functionally silent area of the brain; where this is not an option vagal nerve stimulation may be considered. Alternatively dietary therapy may be considered. Ketogenic dietary therapy has been shown to be as effective as any newer antiepileptic medication in the treatment of children with drug resistant epilepsy, but may be justified as an earlier treatment of choice in specific circumstances. Genetic diagnoses are increasing our understanding of underlying causes of the epilepsies, and in some circumstances allowing a more targeted approach to therapy.

## INTENSIVE CARE MANAGEMENT OF ACUTE ENCEPHALOPATHY AND ACUTE ENCEPHALITIS

#### Sunit SINGHI

Department of Pediatrics, MM Institute of Medical Sciences and Research, MM University, Mullana-Ambala, India

Acute Encephalitis and encephalopathy causes considerable morbidity and mortality worldwide. The goal of intensive care in these conditions is to improve outcomes by limiting secondary brain injury. While no dedicated data exist, in our ICU over 2 years of 316 patients with CNS infections, 56.6% were ventilated, 55%) had a CVP line, 23.1% had ICP monitoring, 43.0% had continuous EEG monitoring and 10% had cerebral function monitoring. The major issues in ICU care are to control systemic factors that affect brain function (i.e., maintaining euthermia, euglycemia, electrolytes, O2 and CO2), treatment of cerebral edema and raised ICP, and control of status epilepticus. The first step in management is airway protection, endotracheal intubation and ventilatory support in unconscious or paralyzed patients, and hemodynamic stabilization. Normoxemia (SpO2 >90%), pCO2 30-35 mm Hg and mean arterial pressure  $\geq 60$  mm Hg are initial targets. Therapy to control seizures (Lorazepam 0.1mg/kg IV, Midazolam 0.25mg/kg IM or Diazepam 0.15mg/kg IV per dose) and raised ICP (mannitol 0.25-1.0 g/Kg bolus) is initiated simultaneously. If seizures persists after benzodiazepine and second-line drugs (IV Fosphenytoin 20mg/kg, Levetiracetam or Sodium Valproate 20-40mg/kg), we use midazolam or valproate infusion under continuous EEG monitoring to control status epilepticus. Immediate neuroimaging is required for suspected raised ICP. Treatment of raised ICP is aimed at achieving optimal cerebral perfusion pressure (CPP) by optimizing circulating volume, vasoactive therapy, hyperosmolar agents (mannitol/3% saline), thiopental and Decompressive craniotomy for refractory ICP elevations. Invasive ICP monitoring is safe and CPP directed therapy improves the outcomes. Monitoring of global and regional brain oxygenation using SjVO2, PbtO2 and NIRS can help in more informed treatment decisions. Specific therapy is added, on basis of clinical suspicion and epidemiological data, for Herpes simplex and Varicella zoster(acyclovir 10 mg/kg IV 8 hourly), mycoplasma (azithromycin), rickettsial infections (doxycycline) or cerebral malaria.

L-30

## L-31 GENERAL MANAGEMENT OF ACUTE VIRAL ENCEPHALITIS/ ENCEPHALOPATHY IN JAPAN

#### Tatsuya KAWASAKI

Department of Pediatric Critical Care, Shizuoka Children's Hospital, Shizuoka, Japan

Acute viral encephalopathy/encephalitis is a fatal disorder with a high incidence of mortality and morbidity, and many such cases have been reported in Asia. Its proposed management in Japan comprises general "supportive" neuro-critical care and "disease-specific" treatments.

Neuro-critical care focuses on the prevention of additional neuronal injuries subsequent to an initial insult on brain parenchyma, such as trauma, ischemic injury, and infection. In general, the secondary injuries include hypoxia and hypoperfusion as well as seizure, pyrexia, hyper/hypoglycemia, and brain edema.

Patients with acute viral encephalopathy/encephalitis almost always present to the emergency departments with consciousness disturbances and, in some cases, hemodynamic instability. The initial management goal is to restore adequate oxygenation and cerebral perfusion. Intubation and ventilation are often required to optimize gas exchange for appropriate cerebral blood flow (CBF). Such patients often need fluid resuscitation to achieve euvolemia initially and sometimes inotropic/vasoactive support later with a restricted maintenance fluid load. A reduction of intracranial pressure should be attempted to facilitate CBF with semi-recumbent positioning and hyperosmolar therapy. Seizures must be suppressed aggressively, often under continuous electroencephalography monitoring, with active control of hyperthemia and glycemic disturbances.

Conversely, the so-called "disease-specific treatments" were suggested in the practice guidelines by the study group of the Ministry of Health of Japan in 2005. The first-line treatment is an antiviral agent. Otherwise, high-dose steroid therapy at an early stage and intravenous immunoglobulins, both intended for hypercytokinemia, are suggested. In addition, the possible efficacy of induced hypothermia, plasma exchange, cyclosporine, and high-dose antithrombin are mentioned. However, all these treatment options are controversial due to the lack of a convincing evidence.

Fortunately, the survival seems to have improved over the past decade. The association of each management component with prognosis improvement should be thoroughly investigated, and evidence-based care needs to be established in the future.

## THERAPEUTIC BRAIN MILD HYPOTHERMIA FOR CHILDHOOD ACUTE ENCEPHALOPATHY

L-32

#### George IMATAKA

Department of Pediatrics, Dokkyo Medical University School of Medicine, Tochigi, Japan

Although previous studies have reported on the effectiveness of brain mild hypothermia therapy in childhood onset acute encephalopathy, additional studies in this field are necessary. In this presentation, we discussed brain hypothermia therapy methods not for two clinical conditions for which sufficient evidences are currently available in the literature but also our clinical data with childhood onset acute

Encephalopathy. The first condition is known as hypoxic-ischemic encephalopathy and occurs in newborns and the second condition is acute encephalopathy which occurs in adults following cardiopulmonary resuscitation associated with out-of-hospital cardiac arrest state resulting from ventricular arrhythmia. But now a days, still not established clinical evidence with acute encephalopathy in childhood.

At the Dokkyo Medical University Hospital, we introduced a brain hypothermia therapy protocol for treating childhood status epilepticus and acute encephalitis/encephalopathy in 2004. Our protocol focuses on infants with a minimum age of six months or 7.5 kg in weight. Applicable diseases include acute encephalitis/encephalopathy occurring from status epilepticus or seizures lasting for 30 minutes or longer, in cases such as near drowning, hypoxic-ischemic encephalopathy, post-resuscitation encephalopathy, cardiorespiratory arrest, severe head injury, or other diagnoses in which the pediatric neurologist recognizes the possibility of neurological complications. Brain hypothermia therapy is managed within the intensive care unit. The target body temperature is a bladder or rectum temperature of 34.0 to 35.0 degrees. This body temperature is reduced to the target temperature within six hours of the seizures. Hypothermia is maintained for 48 hours and concomitant steroid pulse therapy may be used at appropriate times. Sodium thiopental is used to sedate and rewarming is carried out at 0.5 degrees per 12 hours. Osmotic diuretics, muscle relaxants and circulatory antagonists may be concomitantly used at appropriate times. Furthermore, we assessed the prospects of applying mild brain hypothermic therapies to acute encephalopathy in children.

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## L-33 THE ROLE OF THERAPEUTIC HYPOTHERMIA FOR EPILEPSY AND AUTOIMMUNE ENCEPHALITIS

### Kuang-Lin LIN<sup>1)</sup>, Jainn-Jim LIN<sup>2)</sup>

- <sup>1)</sup> Division of Pediatric Neurology, Chang Gung Children's Hospital and Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Taoyuan, Taiwan
- <sup>2)</sup> Division of Pediatric Critical Care and Pediatric Neurocritical Care Center, Chang Gung Children's Hospital and Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Taoyuan, Taiwan

Refractory status epilepticus is an important cause of mortality and neurological deficits during childhood. Although several medical treatment strategies have been proposed including anti-cytokine agents, antiepileptic drugs and treatment to reduce intracranial pressure, the efficiency of these treatment options is certainly limited and not proven in clinical trials. Nevertheless, few studies have reported that therapeutic hypothermia resulted in fast and sustained control of refractory status epilepticus.

The mechanism of therapeutic hypothermia for refractory status epilepticus and autoimmune encephalitis is complex, but it likely has a physiological role. The clinical application of therapeutic hypothermia is based on the possibility of stabilizing immune activation, brain edema and seizure control to protect the brain from on-going functional, apoptotic neural and glial damage and the systemic expansion of the cytokine storm. Therapeutic hypothermia has been shown to have neuro-protective as well as antiedematous effects in various models of neurological damage. The combination of therapeutic hypothermia and conventional medical treatment was effective in treating refractory status epilepticus. However, the exact contribution of the therapeutic hypothermia to the outcome is unknown.

The optimum temperature and duration of therapeutic hypothermia for refractory status epilepticus have been reported to be cooling to 32 to 35°C continuously for 2 to 5 days. Hemodynamic change due to myocardial depression, arrhythmias, coagulopathy, electrolyte imbalance and infection were the possible complications of therapeutic hypothermia.

### REHABILITATION AND COMPREHENSIVE INTERVENTION FOR ACUTE ENCEPHALITIS/ENCEPHALOPATHY IN CHILDHOOD

L-34

#### Hiroshi ARAI, Satori HIRAI

Department of Pediatric Neurology, Morinomiya Hospital, Osaka, Japan

Neurological and developmental outcomes of acute encephalopathy depend on the type of encephalopathy, severity of the brain damage, and the age at the onset. Long-term interventions should be individualized and provided by a multi-disciplinary team, because early brain damage causes various impairments of physical, perceptual, and higher brain function. Typical developmental outcomes and rehabilitation approaches of three types of encephalopathy are introduced in this section. [AESD] Spastic or dystonic state diminishes in a few weeks, and hypotonic state succeeds. Though various hyperkinetic movements become apparent at that phase, they are essentially exaggerated voluntary movements modified by truncal hypotonia. Intensive physical intervention combined by reduction of muscle relaxants or hypnotics is necessary (~6 months). When the affected children become able to hold their heads up earlier than two months from the onset, the target of intervention should be switched from physical function to cognitive and communicative function, because they will be able to walk independently within two years. In order to improve school life and social participation supporting impaired function of frontal and parietal lobes, advice to nursery and school based on full assessment of intellectual and learning ability is necessary. [HSE] Long-lasting severe spasticity and dystonia cause contracture and deformity. Even continual physical therapy and use of muscle relaxants often fail to prevent hip dislocation and scoliosis. Intramuscular botulinum toxin injection or intrathecal baclofen injection is effective. Orthosis and seating instruments should be introduced early for the adequate management of daily posture. [HIE] Watershed infarction and ischemic change of basal ganglia causes mild to moderate physical and intellectual impairment, and ability to walk is determined within 6 months from the onset. Early intensive rehabilitation is desirable. More extended brain damage leads to severe spasticity and rigidity, and the goal of rehabilitation is prevention of secondary impairment.

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# ABSTRACTS

**Oral Presentation** 

## G-01 EFFECT OF OCIMUM BASILICUM HYDROALCOHOLIC EXTRACT AGAINST PENTYLENTETRAZOLE-INDUCED SEIZORE IN ANIMAL MODEL

Mehrdad MODARESI<sup>1)</sup> - Arezoo POURIYANZADEH<sup>2)</sup>

<sup>1)</sup> Biology Faculty, Isfahan (Khorasgan) Branch, Islamic Azad University, Isfahan, Iran

<sup>2)</sup> Biology Faculty, Payam e Noor University – Isfahan Center, Isfahan, Iran

**Objectives**: Seizure always noticed as a most important nerves disease. Notwithstanding using various drugs, still there are many patients resister to this drugs also all of these drugs have harmful effects. In traditional medicine, Ocimum basilicum used to treatment seizure and effects of anticonvulsant of this drug is reported.

**Methods**: In this experimental research, 48 mature mice were divided into 6 groups. To access this anti-seizures drug with low imposition we survey effect of anticonvulsant drug of extract of Ocimum basilicum in seizure induced with pentylenetetrazole. Hydroalcohol extract of Ocimum basilicum with physiologic serum and various dozes (100, 250, 300 and 350 mg/kg) of extract inject to mices via interperitoneal 65 minutes before injection of pentylenetetrazole. And survey factors onset time of showing seizure effects, number of showing seizure effects. The results using the Tukey test, ANOVA and Duncan analysis was performed in SPSS 11.5 software.

**Results**: Results of using various dozes (100 - 250 - 300 - 350 mg/kg) shows that onset time of showing seizure effects, number of showing seizure effects and the percentage of dead at 250 mg/kg doze, 65 minutes before injection of pentylenetetrazole dependently (p<0.05) sequencely increased, decreased and decreased.

**Conclusions**: The results can be obtained at a dose of hydro alcoholic 250 mg/kg effective as medication in preventing seizures in animal models introduced.

Key words: Seizure, Ocimum basilicum, Hydro alcoholic Extract

#### SEIZURES FOLLOWING CHILDHOOD IMMUNIZATION RARE IN BANGLADESH, A COMPREHENSIVE COHORT STUDY

#### Mir ANWAR

Department of Health, South Africa

**Background:** Bangladesh is one of the less developing country in 3<sup>rd</sup> world. Update modern medication was not available in early 90's both in private and public sectors. EPI vaccination program was limited to BCG, DPT, Oral Polio & Measles vaccine only.

**Objective:** To study any vaccine related Febrile or Non Febrile convulsion among all the children vaccinated. And reported to the department of Public Health. As in 1990's It was hot topic that period of time that, post pertussis vaccination cause childhood convulsion especially in the Western Europe.

**Methods:** We chose three busy child clinics in Dhaka City of Bangladesh both government and Private over a period of two years (1990-1992). Total over 5000 children were vaccinated during that time in that three particular centre, we recorded all of them. Age – New born to one year.

**Results:** BCG was given at the 1<sup>st</sup> week of life, DPT and oral polio was started at 6 weeks of life then with a interval of one month three more vaccine was given. At 9 months of age measles vaccine was given. At one year of age booster dose of DPT & Polio was given. Hepatitis B vaccine was excluded in this study, as it was not included in the EPI program that time. We recorded all the side effects and the complications of post vaccination.

**Conclusions:** Our aim of study to record any febrile convulsion or vaccine related convulsion amongst the children, so that we report and recommended to the Department of Public Health. It was hot topic that period of time that, post pertussis vaccination cause childhood convulsion especially in the Western Europe.

Over two years of time out of 5000 infants vaccinated we did not record any Convulsion amongst them. Vaccine related other effects and side effects and complication I will discuss in the talk.

### G-03 FEVER ACTIVATES MICROGLIA TO ENGULF INHIBITORY SYNAPSES AND LOWER THE SEIZURE THRESHOLD

<u>Ryuta KOYAMA</u><sup>1)</sup>, Yuka KASAHARA<sup>1)</sup>, Kazuki SHIBATA<sup>1)</sup>, Sakiko UJITA<sup>1)</sup>, Shota SUGIO<sup>2)</sup>, Kenji F TANAKA<sup>3)</sup>, Koji SHIBASAKI<sup>2)</sup>, Yuji IKEGAYA<sup>1)</sup>

- <sup>1)</sup> Laboratory of Chemical Pharmacology, Graduate School of Pharmaceutical Sciences, The University of Tokyo, Tokyo, Japan
- <sup>2)</sup> Department of Molecular and Cellular Neurobiology, Gunma University Graduate School of Medicine, Gunma, Japan
- <sup>3)</sup> Department of Neuropsychiatry, Keio University School of Medicine, Tokyo, Japan

Fever (typically greater than 38°C)-induced febrile seizures are the most common type of seizures in early childhood. Prolonged febrile seizures could afterwards initiate the development of acute encephalopathy consisting of a cluster of seizures and postictal coma, which is often followed by the development of epilepsy. The induction of delayed seizures after febrile seizures indicates the prolonged impairment in the excitatory versus inhibitory balance (E/I balance) of synapses; however the cellular and molecular link between hyperthermia and E/I imbalance is missing.

Here we report that microglia, the brain-resident immune cells, disrupt the synapse E/I balance in dentate circuits with the phagocytic capacity. Microglia detected the increase in brain temperature during experimental febrile seizures by the Ca2<sup>+</sup>-influx through activation of transient receptor potential vanilloid 4 (TRPV4), which is a thermosensor (activated by  $>34^{\circ}$ C). The TRPV4-mediated Ca2<sup>+</sup>-influx led microglia to preferentially engulf inhibitory synapses, resulting in a decrease of the density of inhibitory synapses in the dentate gyrus.

Finally, minocycline, an inhibitor of microglial activation, decreased the delayed seizure severity after febrile seizures. Thus, our study provides a novel mechanism by which the brain hyperthermia impairs the synapse E/I balance via activation of microglia.

#### CEREBROSPINAL FLUID NEOPTERIN AND CYTOKINE ANALYSIS IN PATIENTS WITH ENCEPHALITIS OR ENCEPHALOPATHY

G-04

Norikatsu HIKITA, Toshiyuki SETO, Kanako YAMASHITA, Kenji FUJITA, and Haruo SHINTAKU

Department of Pediatrics, Graduate School of Medicine, Osaka City University, Osaka, Japan

**Objective:** To find optimal biomarkers to distinguish encephalitis (or encephalopathy) from complicated febrile seizures that lead to decreased consciousness, we retrospectively analyzed the levels of neopterin and various cytokines in the cerebrospinal fluid (CSF) of patients with these diseases.

**Methods:** The subjects were 28 patients who visited the Osaka City University hospital or collaborative hospitals enrolled from April 2010 to January 2016. Ten patients were diagnosed with encephalitis or encephalopathy (group EN), 9 had febrile seizures (group FS), and 9 were controls (group CO). Their cell counts, and levels of neopterin and other 17 kinds of cytokines and chemokines in the CSF were analyzed.

**Results:** Three EN patients showed CSF pleocytosis. Neopterin, IL-6, IL-7, IL-8, G-CSF, GM-CSF, MIP-1b, and TNF-alfa levels were significantly elevated in the EN group, compared to the CO group. IL-8, G-CSF, GM-CSF, MIP-1b levels were significantly higher in the FS group than in the CO group. When comparing the EN and FS groups, only the neopterin level was significantly higher in the EN group than in the FS group. Six of 7 patients in the EN group who did not have pleocytosis showed high neopterin levels, more than 30 nM, compared to only one patient who showed a neopterin level higher than 30 nM in the FS and CO groups combined.

Four EN patients with neurological complications showed neopterin levels much higher than 90nM.

**Conclusions:** In our study, neopterin showed high levels in the EN group, serving as a promising biomarker to distinguish encephalitis or encephalopathy from complicated febrile seizures and may relate with the severity of encephalitis or encephalopathy.

### G-05 IDENTIFICATION OF BIOMARKER FOR EARLY DIAGNOSIS OF AESD BY CSF PROTEOMICS ANALYSIS

<u>Karin KOJIMA</u><sup>1)</sup>, Kenji KUROIWA<sup>2)</sup>, Takahiro IKEDA<sup>1)</sup>, Hiroshi SAKUMA<sup>3)</sup>, Jun-ichi TAKANASHI<sup>4)</sup>, Masashi MIZUGUCHI<sup>5)</sup>, Hitoshi ENDO<sup>2)</sup>, Takanori YAMAGATA<sup>1)</sup>

<sup>1)</sup> Department of Pediatrics, Jichi Medical University, Shimotsukeshi Tochigi, Japan

- <sup>2)</sup> Department of Biochemistry, Jichi Medical University, Shimotsukeshi Tochigi, Japan
- <sup>3)</sup> Department of Brain Development and Neural Regeneration, Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan
- <sup>4)</sup> Department of Pediatrics, Tokyo Women's Medical University Yachiyo Medical Center, Tokyo, Japan
- <sup>5)</sup> Department of Developmental Medical Sciences, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

**Introduction:** Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is clinically characterized by early prolonged febrile seizure followed by late clustering seizures that occur after 3-5 days. Patients with AESD often have severe neurological sequelae. Because there is no biomarker to predict the development of AESD thus far, it is difficult to diagnose AESD in the early phase. The aim of this study was to identify potential biomarkers that were differentially expressed in cerebrospinal fluid (CSF) between AESD patients and monophasic encephalopathy patients, soon after the first seizure.

**Methods:** We analyzed the CSF from AESD patients (n=3) and monophasic encephalopathy patients (n=3). The CSF was collected within ten hours from first seizures. Comparative proteomic analysis of these CSFs was performed by two-dimensional fluorescence difference gel electrophoresis (2D-DIGE) and proteins were identified by MS/MS ion search using LC-MS/MS.

**Results:** In the CSF from AESD patients, six proteins were increased and four proteins were decreased. Of the increased proteins, five were immunoglobulin and one was an antigen involved in the immune response. On the other hand, the decreased proteins were involved in the apoptosis, immune responses and nerve repair.

**Conclusions:** It has been considered that the pathological mechanism of AESD was the neuronal excitotoxicity, however, our data suggested immune responses were also involved in the mechanism.

### GENETIC PRDISPOSITION TO ACUTE ENCEPHALOPATHY WITH STATUS EPILEPTICUS



<u>Makiko SAITOH</u><sup>1</sup>, Ai HOSHINO<sup>1</sup>, Atsushi ISHII<sup>2</sup>, Yukiko IHARA<sup>2</sup>, Shinichi HIROSE<sup>2</sup>, and Masashi MIZUGUCHI<sup>1</sup>

<sup>1)</sup> Department of Developmental Medical Sciences, The University of Tokyo, Tokyo, Japan

<sup>2)</sup> Department of Pediatrics, Fukuoka University, Fukuoka, Japan

**Objective:** Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is prevalent in East Asia, and presents initially with status epilepticus in most cases. The etiology of AESD remains unclear, but likely involves both genetic and environmental factors. To elucidate the genetic background of AESD, we examined polymorphism of candidate genes deduced from its pathomechanism.

**Methods:** We recruited 85 Japanese patients with AESD. We genotyped polymorphisms of the carnitine palmitoyl transferase 2 (*CPT2*) and adenosine receptor genes (*ADORA1* and *ADORA2A*) and compared their frequency between the patients and controls. We also screened mutations of voltage-gated sodium channel genes (*SCN1A* and *SCN2A*).

**Results:** For *CPT2*, the frequency of G allele at rs2229291c.1055T>G (p.F352C) was significantly higher in the patients than in controls (p = 0.013, OR2.09, CI=1.22-3.57). The amino acid substitution from F to C reportedly diminished the CPT2 activity. Complete linkage of four SNPs in *ADORA2A* resulted in only two haplotypes (A and B). We found that Haplotype A was associated with an increased risk of AESD (OR 1.70, 95%CI 1.17-2.45, p = 0.005). *ADORA2A* mRNA expression in lymphoblasts with diprotype AA was higher than those in AB and BB. Diprotype AA showed the highest production of cyclic AMP, suggesting the involvement of the adenosine/cAMP signal cascade in the pathogenesis of AESD. We found that 5.4% of AESD patients had missense variants of either *SCN1A* or *SCN2A*. Two variants, R1575C in *SCN1A* and F328V in *SCN2A*, are occasionally found (around 0.1%) in normal East Asian, but not in other population, which may account for the high incidence of AESD in Japan.

**Conclusion:** We demonstrated *CPT2 and ADORA2A* polymorphisms, and variants in *SCN1A* and *SCN2A* are one of the predisposing factors of AESD. These findings showed the involvement of multiple genetic factors in AESD.

#### G-07 HLA VARIANTS AND CYTOKINE GENE POLYMORPHISMS CONFER SUSCEPTIBILITY TO ACUTE NECROTIZING ENCEPHALOPATHY

<u>Ai HOSHINO</u><sup>1), 4)</sup>, Makiko SAITOH<sup>1)</sup>, Masaya KUBOTA<sup>2)</sup>, Jun-ichi TAKANASHI<sup>3)</sup>, Akira OKA<sup>4)</sup>, Masashi MIZUGUCHI<sup>1)</sup>

- <sup>1)</sup> Department of Developmental Medical Sciences, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan
- <sup>2)</sup> Division of Neurology, National Center for Child Health and Development, Tokyo, Japan
- <sup>3)</sup> Department of Pediatrics, Tokyo Women's Medical University Yachiyo Medical Center, Yachiyo, Japan,
- <sup>4)</sup> Department of Pediatrics, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

**Purpose:** Acute necrotizing encephalopathy (ANE) is a fulminant type of acute encephalopathy following infectious diseases, prevalent in young children in East Asia. Although the pathogenesis remains unclear, cytokine storm is considered as the main pathogenesis leading to neuronal death and multiple organ failure. In this study, we investigated host genetic factors of innate immunity rendering Japanese patients susceptible to ANE.

**Methods:** We recruited 32 Japanese ANE patients (16 males and 16 females, aged from 7 months to 9 years and 7 months). We examined the positivity of HLA genotypes and SNPs at the promoter region of *IL6* and *IL10*. Phorbol myristate acetate-induced cytokine production was analyzed in each *IL6* and *IL10* genotype lymphoblasts cell line by Bio-Plex system.

**Results:** We detected a significant association of *HLA-DRB1\*0901* and *DQB1\*0303* with ANE (p=0.04 and p=0.03, respectively). These genotypes are reportedly associated with multiple autoimmune diseases in Japanese, such as type I diabetes mellitus, juvenile myasthenia gravis and polyangiitis. Genotype distributions of *IL6 -572* C/G and *IL10* (-819,-627) T/C, A/C were significantly different between ANE and controls (p=0.02 and p<0.01, respectively). *IL10 -*819 and -627 SNPs are completely linked, which resulted in three diplotypes, TA/TA, TA/CC and CC/CC. Diplotype CC/CC frequency was higher in ANE (21.9%) than in controls (8.4%). IL10 production was significant lower in cells with diplotype CC/CC than in those with TA/TA.

**Conclusions:** We found multiple genetic factors of innate immunity associated with Japanese ANE. *HLA-DRB1\*0901 -DQB1\*0303* diplotype is common in Asian populations, but is rare in European, which may account for the high prevalence of ANE in Asia. The pathogenesis of ANE may involve the unbalanced cytokines production due to cytokine gene polymorphism.

#### EARLY ONSET EPILEPTIC ENCEPHALOPATHY -AN UNUSUAL PHENOTYPE WITH MULTISYSTEM INVOLVEMENT RELATED TO A PATHOGENIC SCN1A MUTATION



Asuri N PRASAD<sup>1</sup>, Andrea ANDRADE<sup>1</sup>, Sarah MCKAY<sup>2</sup>, Victoria SIU<sup>3</sup>

- <sup>1)</sup> Department of Pediatrics & Division of Clinical Neurosciences, Western University and London Health Sciences Centre, London, Ontario, Canada
- <sup>2)</sup> Nurse Practitioner, Complex Care Program, London Health Sciences Centre, London, Ontario, Canada
- <sup>3)</sup> Medical Genetics program of South Western Ontario, Western University and London Health Sciences Centre, London, Ontario, Canada

**Objective:** Early onset epileptic encephalopathy (EIEE) is an electroclinical syndrome with a poor prognosis. The objective is to describe a unique presentation with video EEG study, genotype phenotype correlation.

**Methods:** We describe a female infant (35 weeks+3 days) presenting with seizures in within hours of birth that progressed to intractable epileptic spasms associated with clinical desaturations, and respiratory distress. The EEG showed excess discontinuity of background rhythms, multifocal spikes, desynchronization followed by electrodecrement accompanying the flexor spasms. Neuroimaging of the brain was normal. Dysmorphic features noted included; epicanthal folds, anteverted nares, hypertelorism, redundant nuchal skin, widely-spaced nipples, relative macrocephaly, edema of extremities, overlapping fingers. X-rays of the lungs showed a ground glass appearance. A scoliosis with left convexity at the thoracolumbar junction (Cobb angle of 34 degrees) was also noted. Cardiac assessment was negative for abnormalities. The epileptic spasms were intractable and frequent (>100 events/day). Treatment resistance to multiple AEDs (phenytoin, phenobarbital, levetiracetam) and seizure aggravation with topiramate was noted. A greater than 50% reduction in seizure frequency was attained on the combination of vigabatrin, stiripentol, and clobazam.

**Results:** Chromosomal microarray (CMA) showed a CNV gain 0.715 Mb of uncertain significance in chromosome region 2q21.2q21.3 containing no OMIM morbid genes. Molecular genetic testing disclosed a heterozygous novel variant c.1261G>A transition (p.Val421met). The substitution occurs at a conserved position in the transmembrane helical segment S3 in the first homologous domain and was scored as carrying a deleterious effect with Polyphen2 and Provean. Parental testing was negative for the variant, suggesting a de-novo change in the infant.

**Conclusion:** The multisystem involvement, intractable epileptic spasms, identification of a pathogenic previously unreported SCN1A mutation and treatment response to stiripentol in combination with Vigabatrin are of interest. This report may be the first of a unique phenotype of EIEE associated with SCN1A mutation.

#### G-09 COMPOUND HETEROZYGOUS PIGT MUTATIONS IN AN INFANT WITH SEVERE DEVELOPMENTAL DELAY AND INTRACTABLE MYOCLONIC SEIZURE

<u>Shohei KUSABIRAKI</u><sup>1</sup>, Akihiko ISHIYAMA<sup>1</sup>, Keisuke KOHASHI<sup>1</sup>, Kenji SUGAI<sup>1</sup>, Masayuki SASAKI<sup>1</sup>, Noboru IGARASHI<sup>2</sup>, Junko MATSUZAWA<sup>3</sup>, Shinichi YAGI<sup>4</sup>

- <sup>1)</sup> Department of Child Neurology, National Center Hospital, National Center of Neurology and Psychiatry, Tokyo, Japan
- <sup>2)</sup> Department of Pediatrics, Toyama Prefectural Central Hospital, Toyama, Japan
- <sup>3)</sup> Department of Child Neurology, Toyama Prefectural Rehabilitation Hospital, Toyama, Japan
- <sup>4)</sup> Toyama Medical Association Pediatrics, Toyama Japan

**Objective:** Glycosylphosphatidylinositol (GPI) acts as the anchor of various proteins expressed on the plasma membrane. Recently, recessive loss-of-function mutations in genes involved in the GPI anchor protein (GPI-AP) biosynthesis pathway have been implicated as causes of GPI deficiency syndromes associated with intellectual disability, seizures, and diverse congenital anomalies.

**Methods:** We performed whole exome sequencing in a 10 month old Japanese male infant with developmental delay, tonic seizure, myoclonic seizure, apnea, and multiple anomalies, including clinodactyly, overlapping finger, pecutus excavatum, cryptorchidism. Functional validation of the mutations was performed by flow cytometry analysis of surface expression of the proteins.

**Results:** We identified compound heterozygous mutations in *PITG*, which encodes a subunit of the PGI transaminase complex, [c.250 G>T, p.Glu84X] and [c.1096 G>T, p.Gly366Trp], the former previously reported and the latter novel. Each of the mutations is transmitted from a heathy nonconsanguineous parent. By flow cytometry, we found that granulocytes from the patient had reduced levels of the GPI-AP, supporting pathogenicity of the mutations. A brain MRI of the patient revealed hypoplasia of the brainstem and the cerebellum. Electroencephalography showed hypsarrhythmia, and he was diagnosed as West syndrome and started on ACTH therapy and several anti-epileptic drugs. However, the epileptic seizures, such as tonic, apneic and myoclonic seizures, were refractory. Although he required multiple admissions for pneumonia, epilepsy, and renal tubular acidosis, he is now three-years-old and has been supported successfully by regional home nursing using tube-feeding and non-invasive positive pressure ventilation.

**Conclusion:** We identified compound heterozygous mutations in *PIGT* in an infant as the cause of GPI-AP deficiency; multiple congenital anomalies-hypotonia-seizures syndrome 3. Further functional studies on additional cases will be needed to elucidate the relevance of such mutations in PIGT function and identify the clinical spectrum and long-term prognosis of disorders belonging to GPI deficiency syndromes.

### A NOVEL KCNQ2 MUTATION IN FAMILIAL EARLY-ONSET EPILEPTIC ENCEPHALOPATHY



<u>Yuan-feng ZHOU</u><sup>1),4)</sup>, Bing-bing WU<sup>2),4)</sup>, Guo-qiang CHENG<sup>3)</sup>, Wen-hao ZHOU<sup>3),5)</sup>, Yi WANG<sup>1),5)</sup>

- <sup>1)</sup> Department of Neurology.
- <sup>2)</sup> The Molecular Genetic Diagnosis Center, Shanghai Key Lab of Birth Defects, Pediatrics Research Institute.
- <sup>3)</sup> Department of Neonatology, Children's Hospital of Fudan University, Shanghai, China.

KCNQ2 gene encoding for voltage-gated potassium channel subunitsKv7.2 and its mutation have been shown to cause benign familial neonatal seizures (BFNS) or epileptic encephalopathy with developmental delay or intellectual disability(ID). Here We report a clinical and Chinese family in which two members were diagnosed with KCNQ2 encephalopathy presenting early onset refractory seizures in the first week of life and neurocognitive deficits . Whole exome sequencing was used to detect the underlying genetic cause. A novel frame shift mutation c. 2422het\_dup T was identified in KCNQ2 in two affected members. Three patients in this family had onset of seizures but the severity of seizures was various and lead to different consequence. These findings suggest that KCNQ2 mutation should be considered in neonates with medicine resistent seizures of unknown cause and contray to previous reports that all mutations published so far are missense mutations , frameshift mutation also can be found in KCNQ2 encephalopathy.

**Key Words:** KCNQ2, Voltage-gated potassium channels, Early onset epileptic encephalopathy, neurocognitive deficit

# G-11 A CASE OF FAMILIAL ACUTE NECROTIZING ENCEPHALOPATHY WITH NOVEL GENE MUTATION FROM INDIA

<u>Prashant Ramesh UTAGE</u>, Vsv PRASAD, Malavika B G, U APARNA, Department of Pediatrics, Lotus Hospital For Women and Children, Hyderabad, India Department of Early Intervention, Utage Child Neuro Clinic and Development Centre, Hyderabad, India

Familial acute necrotizing encephalopathy (FANE) typically affects young, healthy children who develop rapid-onset severe encephalopathy triggered by viral infections. We report the details of a Familial ANE among 3 siblings of a family who presented with similar clinical complaints and were diagnosed to have ANE. Brain magnetic resonance imaging abnormalities were found in bilateral thalami including cerebellum which were characteristic of ANE in 2 siblings. Both the patient and his father, who was asymptomatic, harbored a heterozygous Ran-binding protein 2 (RANBP 2) variation. Our case suggests that newer mutations are possible and resulted in familial pattern of the disease. The parent despite harboring the heterozygous mutation was asymptomatic. Positive family history can aid in early recognition of the condition when presents in a similar fashion which may lead to better treatment options.

Case report: A previously healthy, 11 month-old male infant who was born of a non consanguineous marriage with uneventful birth history was developmentally normal till the onset of present illness. He was referred to us with history of fever, cold and cough of 1 day duration followed by multiple episodes of generalized tonic clonic seizures – status epilepticus and altered sensorium. Family history suggested sibling deaths with similar presentation. On admission, he was afebrile with stable vitals. His GCS was E2V4M5 with pupils bilaterally equal reactive to light. He had bilateral brisk deep tendon reflexes with ankle clonus. Infection and neurometabolic screen were unremarkable with mild elevation in transaminases. He was started on IV Methylprednisolone on day 1 of admission in view of family history suggestive of ANEC. MRI brain was done which showed bilateral symmetric involvement of olivary nuclei in medulla, pontine white matter, cerebellar dentate nuclei, thalami, posterior putamina, internal capsule, external capsule and hemispheric white matter in T2 images with hypointensities of the corresponding lesions in T1 axial images. Contrast enhanced T1 images showed central necrotic zones within the lesions in the thalami, putamina and pons. Diffusion restriction was noted in bilateral thalamic regions. Susceptibility weighted images showed hemorrhages in bilateral thalamic regions.

Genetic testing showed heterozygous missense variation in exon 20 of the RANBP2 gene (chr2:109382244; C>C/G) that results in the amino acid substitution of Arginine for Proline at codon 1750 (p.P1750R; ENST00000283195). Parental genetic testing in the form of Segregation analysis was done which indicated the presence of the heterozygous missense RANBP2 variation in the father that was detected in the proband. Segregation analysis of the mother indicated the absence of the heterozygous missense RANBP2 variation that was detected in the proband.

#### ELECTROENCEPHALOGRAM FINDINGS IN ACUTE EVCEPHALITIS/ ENCEPHALOPATHIES

<u>Tatsuya FUKASAWA</u><sup>1)</sup>, Akihisa OKUMURA<sup>2)</sup>, Takeshi SUZUKI<sup>1)</sup>, Yuji NAKAMURA<sup>3)</sup>, Misa MIYAKE<sup>4)</sup>, Atsuko OHNO<sup>5)</sup>, Tetsuo KUBOTA<sup>1)</sup>, Takeshi TSUJI<sup>6)</sup>, Naoki ANDO<sup>7)</sup>, Shinji SAITOH<sup>7)</sup>, and Jun NATSUME<sup>5)</sup>

<sup>1)</sup> Department of Pediatrics, Anjo Kosei Hospital, Anjo, Japan

- <sup>2)</sup> Department of Pediatrics, Aichi Medical University, Nagakute, Japan
- <sup>3)</sup> Department of Pediatrics, Toyohashi municipal hospital, Toyohashi, Japan
- <sup>4)</sup> Department of Pediatrics, Fujita Health University School of Medicine, Toyoake, Japan
- <sup>5)</sup> Department of Pediatrics, Nagoya University, Nagoya, Japan
- <sup>6)</sup> Department of Pediatrics, Okazaki City Hospital, Okazaki, Japan
- <sup>7)</sup> Department of Pediatrics and Neonatology, Nagoya City University, Graduate School of Medical Sciences, Nagoya, Japan

**Objective:** Acute encephalitis/encephalopathies include various conditions with a variety of abnormal electroencephalogram (EEG) findings. In this study, we investigated interictal EEG findings in acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) and clinically mild encephalitis/encephalopathy with reversible splenial lesion (MERS), two clearly defined subtypes.

**Methods:** This study enrolled 22 patients with AESD and 21 with MERS registered in the Tokai Pediatric Neurology Society database between 2009 and 2015 who underwent EEG within 5 days of onset. We examined focal or diffuse slowing, spindle formation, fast waves, and paroxysmal discharges. Three patients with AESD and six with MERS whose EEG record included no sleep records were excluded from the estimation of spindle formation.

**Results:** Of the 22 patients with AESD, 9 underwent EEG before the seizures at the second phase and 13 patients after the secondary seizures. Focal or diffuse slowing, abnormalities in spindle formation, excessive fast waves, a decrease in fast waves, and paroxysmal discharges were observed in 15 (68%), 17 (89%), 5 (23%), 8 (36%), and 2 (9%) patients with AESD and in 19 (86%), 3 (19%), 3 (14%), 0 (0%), and 1 (5%) patients with MERS, respectively. Abnormalities in spindle formation and a decrease in fast waves were observed significantly more frequently in AESD than in MERS (both p < 0.01). No patients with AESD and 3 (14%) patients with MERS had normal EEG records.

**Conclusion:** All of the patients with AESD, including those whose EEGs were recorded before seizures at the second phase, had some abnormal EEG findings. Abnormalities in spindle formation and a decrease in fast waves were observed more frequently in AESD than in MERS. EEG is sufficiently sensitive to detect abnormalities in AESD even before seizures at the second phase and may show findings that reflect the pathology.

### G-13

### THE CASE OF CLINICO-ELECTRICAL DISSOCIATION OF ENCEPHALOPATHY

Soichiro TODA<sup>1)</sup>, Shota YUASA<sup>1)</sup>, Jun-ichi TAKANASHI<sup>2)</sup>, and Hiroshi SAKUMA<sup>3)</sup>

<sup>1)</sup> Department of Pediatrics, Kameda Medical Center, Chiba, Japan,

<sup>2)</sup> Department of Pediatrics, Tokyo Womens Medical University Yachiyo Medical Center, Tokyo, Japan

<sup>3)</sup> Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan

**Introduction:** Patients with encephalopathy usually show impaired consciousness, and often show high voltage slow waves (HVS) in electro-encephalography (EEG). HVS usually disappear as patients become alert. We experienced a case of anti-neuronal antibodies (ANA) positive encephalopathy with persistent HVS, even after patient became alert after initiation of therapy.

**Case:** Previously healthy 5 year-old-girl presented with general tonic-clonic status epilepticus with fever showed impaired consciousness and abnormal behavior. She showed normal cerebro-spinal fluid (CSF) and brain MRI findings but showed HVS. Abdominal ultra sound showed no ovarian cyst. We diagnosed her with encephalopathy and started steroid pulse therapy from the 2nd day. She became alert on the 5th day, but HVS remained by 81st day. Brain MRI on the 4th and 9th day was normal. We started carbamazepine and valproate as she developed tonic-clonic seizure on the 8<sup>th</sup>, 9<sup>th</sup>, and 14<sup>th</sup> day. EEG normalized after 10 months from onset. Some serum and CSF ANA were positive but we could not specify their types. Viral PCR of pharynx and CSF were negative. Some serum ANA remained positive even after 5 months from onset.

**Discussion:** We suspected of some autoimmune encephalopathy with persistent HVS. As ANA remained positive even during a recovery stage, her neuronal symptoms may be explained by ANA affecting central nervous system as infection collapsed blood brain barrier.

#### TRANSIENTLY REDUCED CORTICAL DIFFUSION IN CHILDREN EXHIBITING PROLONGED FEBRILE SEIZURES



<u>Takeshi SUZUKI</u><sup>1)</sup>, Tetsuo KUBOTA<sup>1)</sup>, Tatsuya FUKASAWA<sup>1)</sup>, Ryosuke SUZUI<sup>2)</sup>, Takeshi TSUJI<sup>2)</sup>, Toru KATO<sup>2)</sup>, Hiroyuki KIDOKORO<sup>3)</sup>, Naoki ANDO<sup>4)</sup>, Akihisa OKUMURA<sup>5)</sup>, Jun NATSUME<sup>3)</sup>

<sup>1)</sup> Department of Pediatrics, Anjo Kosei Hospital, Anjo, Japan

<sup>2)</sup> Department of Pediatrics, Okazaki City Hospital, Okazaki, Japan

<sup>3)</sup> Department of Pediatrics, Nagoya University, Nagoya, Japan

<sup>4)</sup> Department of Pediatrics and Neonatology, Nagoya City University, Nagoya, Japan

<sup>5)</sup> Department of Pediatrics, Aichi Medical University, Nagakute, Japan

**Objective:** Although many reports have shown that status epilepticus patients exhibit reduced cortical diffusion, few reports have addressed abnormal changes in the diffusion-weighted images (DWIs) of patients exhibiting prolonged febrile seizures (PFSs). We have encountered some cases that have exhibited a transient reduction in cortical diffusion after PFSs, but they did not require any treatment and were discharged with no sequelae. We evaluated the clinical features of such patients in comparison with those of patients who did not exhibit signal changes.

**Methods:** We retrospectively collected clinical data on patients who visited the emergency rooms of two hospitals (Anjo Kosei Hospital and Okazaki City Hospital) with PFSs from January 2013 to December 2014. We analyzed patient age, the extent of consciousness impairment evident 6 h after seizure onset, the extent of seizure control, serum AST level, serum Na level, and electroencephalographic features. We studied patients who did and did not exhibit a reduction in diffusion.

**Results:** We studied 40 PFS patients, of whom 28 underwent head MRI in the emergency room. None of these patients were diagnosed with acute encephalopathy (including AESD), but one of the remaining 12 patients was finally diagnosed with AESD. Six patients exhibited cortical areas of abnormally high signal intensity on DWIs. Follow-up MRI scans were performed 13-67 h after seizure onset. All signal changes had disappeared by that time. We found no significant differences between the clinical data of the two groups (those who did and did not exhibit signal changes).

**Conclusion:** Some PFS patients exhibit transient reductions in diffusion soon after seizure onset. These patients obviously differ from those with encephalopathy in terms of clinical course. It is important to bear in mind that some PFS patients present with focally abnormal DWI findings in the very early phase of disease; these disappear rather rapidly.

### G-15 LONGITUDINAL BRAIN MRI PATTERN IN JAPANESE ENCEPHALITIS

<u>Yukie ARAHATA</u><sup>1</sup>, Katsunori FUJII<sup>2</sup>, Tatsuya NISHIMURA<sup>1</sup>, Katsuhiko KITAZAWA<sup>1</sup>, and Akihito HONDA<sup>1</sup>

<sup>1)</sup> Department of Pediatrics, Asahi General Hospital, Chiba, Japan

<sup>2)</sup> Department of Pediatrics, Chiba University Graduate School of Medicine, Chiba, Japan

**Objective:** Japanese encephalitis virus (JEV) causes an important zoonotic vector-borne disease first isolated from a human in Japan in 1935. Although JEV is considered to be the most frequent viral encephalitis associated with fatal or severe outcomes, longitudinal change of brain lesions using MRI has not been well described. Here, we demonstrate longitudinal MRI patterns of a 10-month-old Japanese boy with Japanese encephalitis with the review of the previous published literature.

**Methods:** We examined longitudinal MRI examination in a 10-month-old Japanese boy associated with JEV infection. He initially exhibited conjugate horizontal gaze and tetraplegia, and his consciousness disturbance continued for a long time. We evaluated his brain lesions by MRI weekly compared with clinical manifestations. We also searched previous reports of Japanese encephalitis on PubMed website using the terms of Japanese encephalitis, Japanese encephalitis virus and JEV.

**Results:** He was diagnosed as having Japanese encephalitis, by detection of JEV RNA in cerebrospinal fluid. Brain lesions were dominantly affected on bilateral thalami, and slightly on basal ganglia. T2 weighted and diffusion images were comparatively sensitive to detect brain lesions. Interestingly, dotted right-side dominant thalamus lesions at the initial stage has been changed to be uniform one, suggesting that these imaging patterns may become a clue to differentiate other diseases such as mitochondrial disorder and hypoxic ischemic encephalopathy. Literature survey revealed 423 literatures on PubMed demonstrating clinical features, viral characteristics and regional epidemiology, but little report of longitudinal brain changes of Japanese encephalitis on CT and MRI.

**Conclusion:** Brain MRI is a useful tool to detect specific thalamic lesions caused by JEV encephalitis. Longitudinal MRI changes of thalamus from spotty to uniform lesions may become a clue to diagnose Japanese encephalitis.

#### CLINICAL PHENOTYPES AND GENETIC FINDINGS IN CHILDREN WITH MITOCHONDRIAL ENCEPHALOPATHIES: STUDY FROM A TERTIARY CARE UNIVERSITY HOSPITAL IN SOUTH INDIA

<u>Bindu Parayil SANKARAN</u><sup>1)</sup>, Sonam K<sup>2)</sup>, Govindaraju C<sup>1)</sup>, Govindaraju P<sup>1)</sup>, Nahid A KHAN<sup>6)</sup>, Shwetha CHIPLUNKAR<sup>2)</sup>, Madhu N<sup>1)</sup>, Arvinda HR<sup>3)</sup>, Gayathri N<sup>4)</sup>, Srinivas Bharath MM<sup>5)</sup>, Vandana NUNIA<sup>6)</sup>, Thangaraj K<sup>6)</sup>, Sinha S<sup>1)</sup>, Taly AB<sup>1)</sup>

<sup>1)</sup> Depts of Neurology, National Institute of Mental Helath And Neurosciences

- <sup>2)</sup> Depts of Clinical Neurosciences, National Instittue of Mental Health & Neurosciences
- <sup>3)</sup> Dept of Neuroimaging and Interventional Radiology, National Institute of Mental Health& Neurosciences
- <sup>4)</sup> Department of Neuropathology, National Institute of Mental Health & Neurosciences
- <sup>5)</sup> Depts of Neurochemistry, National Institute of Mental Health & Neurosciences, Bangalore, India
- <sup>6)</sup> CSIR-Centre for cellular and molecular Biology

**Background:** Establishing a definite diagnosis in children with mitochondrial disorders is a challenge because of the dual genome origin, multisystem manifestations and an ever increasing spectrum of phenotypes and genotypes. The clinical profile and genotypes in children with mitochondrial disorders from India are largely unexplored.

**Patients & Methods:** Over a period of 8 years (2006-2013), 250 children underwent comprehensive evaluation for suspected diagnosis of mitochondrial disorder including sequencing of complete mitochondrial genome and selected nuclear genes (*POLG1*, *SURF1*). Twenty three patients also underwent targeted exome sequencing. Patients were recruited into the study when they satisfied the clinical criteria of mitochondrial disorder as suggested by Bernier et. Al.

**Results:** There were 30 children (Age range, 8mo-17yrs; M:F:: 1.3:1) with a definite genetic diagnosis of mitochondrial disorders. Consanguinity was noted in 50% and family history in 46%. Syndromic diagnosis was made in 22 (Leighs syndrome, n=9; Mitochondrial encephalomyopathy lactic acidosis and stroke like syndrome (MELAS, n=6); Myoclonic epilepsy ragged red fiber syndrome (MERRF, n=2); Mitochondrial spinocerebellar ataxia epilepsy syndrome (MSCAE,n=2); Sensory ataxic neuropathy dysarthria ophthalmoplegia syndrome (SANDOS) and LHON plus syndrome one each). Histopathology showed definite evidence of mitochondrial dysfunction in 13/25 and respiratory chain complex deficiency was seen in 18/17 (Multiple complex deficiency, n=10; Complex IV, n=6; Complex 1,n=2). The genotypes included mitochondrial point mutations (n=14, m.3243 A>G (n=6), M.8334 A>G (n=2), m.8362 T>G (n=2) and m.11778 G>A, m.13513 G>A m.13514 A>G, m.8363G>A one each) and nuclear mutations (n=16, *SURF1= 7, POLG1=4, NDUFA1, SERAC1, EARS2, SUCLA-2 & COX-15* one each.)

**Conclusion:** This study highlights the heterogenous clinical and genetic findings in children with mitochondrial encephalopathies. Exome sequencing is a useful tool in elucidating the genetic etiology in children with mitochondrial disorders.

#### G-17 BRAIN MRI AND ITS CONSECUTIVE EPILEPTIC SEIZURES IN A BOY WITH ORNITHINE TRANSCARBAMYLASE DEFICIENCY AND PATERNAL LIVER TRANSPLANTATION

#### Tatsuro IZUMI

Department of Pediatrics and Child Neurology, National Nanao Hospital, Nanao, Japan

Ornithine transcarbamylase deficiency (OTCD) is the most common inborn error of metabolism of the urea cycle. The most severe clinical form of OTCD occurs in fullterm male neonates who appear healthy for 24-48 hours and then exhibits signs of acute progressive lethargy, apnea and seizures as an acute hyperammonemic encephalopathy and cerebral edema. Liver transplantation is a successful and definite treatment for patients who have been well controlled, and then avoides hyperammonemic crisis any more.

Case report: This boy is a first product of healthy Japanese parents without any family history of neurological and metabolic disorder. He was vaginally delivered at term without any complication, GA 39 weeks-2,854g. He presented at the age of 3days with lethargy, vomiting, respiratory distress, and progressing to coma and apnoic generalized clonic seizures, and need for ventilatory assist. Elevated blood ammonia levels as high as 10,160µg/dl were found, which need intensive hemodialysis. DNA analysis revealed the mutation of Ex6,c.626C>T, p.A209V in the OTC gene. He underwent paternal vivifying liver transplantation at the age of 11 months. Since the transplantation, he has not any episode of hyperammonemia, but had failure to thrive, microcephalus, hypertonia, severe neurodevelopmental deteriorations and intractable multifocal epileptic seizures. MRI at the age of 47 days demonstrated multiple, bilateral, symmetrically placed cystic lesions at the cortical gray-white matter junction in occipital, parietal and temporal lobes, and also insular cortex, cingulate gyri and corpus striatum. Ictal EEG at age of 5 years 3 months presented diffuse polyspikes bursts associated with downbeat nystagmus, and spike/spikewave bursts on right frontal region, followed to bilateral frontal and frontopolar regions, associated with right deviation and staring of eye balls.

These aggregate clinical picture might be consisted with the MRI in infancy after hyperammonemic encephalopathy. Liver transplantation should be done, if possible, before hyperammonemic crisis.

### PROCALCITONIN LEVEL IN ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION



<u>Michihiko TAKASU</u><sup>1)</sup>, Hirokazu KURAHASHI<sup>1)</sup>, Jun NATSUME<sup>2)</sup>, Shinji SAITO<sup>3)</sup>, Takeshi TSUJI<sup>4)</sup>, Tetsuo KUBOTA<sup>5)</sup>, Motomasa SUZUKI<sup>6)</sup>, Yoshiteru AZUMA<sup>2)</sup>, Akihisa OKUMURA<sup>1)</sup>

<sup>1)</sup> Department of Pediatrics, Aichi Medical University Graduate School of Medicine, Aichi, Japan

<sup>2)</sup> Department of Pediatrics, Nagoya University Graduate School of Medicine, Aichi, Japan

<sup>3)</sup> Department of Pediatrics, Nagoya city University Graduate School of Medicine

<sup>4)</sup> Department of Pediatrics, Okazaki City Hospital, Okazaki, Japan

<sup>5)</sup> Department of Pediatrics, Anjo-kosei Hospital, Aichi, Japan

<sup>6)</sup> Department of Pediatric neurology, Aichi Children's Health and Medical center, Aichi, Japan

**Objective:** Acute encephalopathy with biphasic seizures and reduced diffusion (AESD) is an encephalopathy characterized by biphasic seizures and late subcortical diffusion abnormalities. The biomarker which is useful for early diagnosis of AESD has not been established. Procalcitonin (PCT) can be elevated by systemic inflammatory response related to innate immunity. We hypothesized that PCT may be useful for the early diagnosis of AESD.

**Method:** We retrospectively collected patients with AESD in which PCT was measured from 2009 to 2015. We compared the PCT levels among AESD, febrile seizure (FS), and febrile status epilepticus (FSE).

**Result:** PCT levels within a day from the onset were higher in AESD (n = 3, median 6.68 ng/ml, range 5.3 - 38.2) compared to FSE (n = 4, median 0.5 ng/ml, range 0.5 - 0.71) and FS (n = 8, median 0.134 ng/ml, range 0.04 - 2.44). Although PCT levels at the second day from the onset were also higher in AESD (n = 3, median 20.4, range 13.4 - 38.2) compared to FSE (n = 7, median 1.29 ng/ml, range 0.3 - 16.1) and FS (n = 2, median 0.69 ng/ml, range 0.5 - 0.69), some patients with FSE had high PCT levels at the second day.

**Conclusion:** Our findings suggested that high PCT level can be useful for early diagnosis of AESD when it was determined immediately after the onset. High PCT level in AESD suggests that innate immunity will be involved in developing AESD.

#### G-19 BIOCHEMICAL AND GENETIC PROGNOSTIC FACTORS IN ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION (AESD)

<u>Hiroshi MATSUMOTO<sup>1</sup></u>, Kiyotaka ZAHA<sup>1</sup>, Yasuko NAKAMURA<sup>1</sup>, Makiko SAITOH<sup>2</sup>, Masashi MIZUGUCHI<sup>2</sup>, and Shigeaki NONOYAMA<sup>1</sup>

<sup>1)</sup> Department of Pediatrics, National Defense Medical College, Tokorozawa, Japan

<sup>2)</sup> Department of Developmental Medical Sciences, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

**Objective:** To investigate the biochemical and genetic prognostic factors in acute encephalopathy with biphasic seizures and late reduced diffusion (AESD).

**Methods:** We reviewed a total of 10 patients who were diagnosed to have AESD in our hospital. The diagnostic criteria of AESD were as follows: (1) prolonged seizures at onset, (2) transient improvement in consciousness followed by recurrence of seizures and deterioration of consciousness, and (3) reduced diffusion in the subcortical white matter on MRI. Serum AST, ALT, LDH, CK, glucose, ferritin, sIL-2R, and urine b2-microglobulin (2-MG) were evaluated as biochemical markers. *CPT2* and *ADORA2A*, of which polymorphisms were proved to associate with the pathogenesis of acute encephalopathy, were also analyzed. The prognosis was evaluated by the cognitive function, gross motor function, and the presence of obvious brain atrophy on MRI.

**Results:** The median age of 10 patients (7 boys, 3 girls) was 16 months. The prolonged seizures (status epilepticus) at onset were seen in 7 patients, and the recurrence of seizures was seen in 9 patients. Obvious brain atrophy was observed in 5 patients, and 3 of them were left with mild to severe cognitive and/or gross motor dysfunctions. The remaining 5 patients showed normal cognitive and gross motor functions. The levels of serum AST, LDH, glucose, and urine 2-MG were higher in 5 patients with brain atrophy. There were no differences in levels of ALT, ferritin, and sIL-2R among AESD patients except for severely affected one. Acute encephalopathy associated gene polymorphisms in *CPT2* and *ADORA2A* were found in 3 and 4 patients, respectively. *ADORA2A* polymorphism was observed in 3 of 5 patients with obvious brain atrophy.

**Conclusion:** High levels of serum AST, LDH, glucose, and urine b2-MG suggested poor neurological outcome in AESD patients. The presence of acute encephalopathy associated *ADORA2A* polymorphism may contribute to the poor neurological outcome.

#### ACUTE NECROTIZING ENCEPHALOPATHY OF CHILDHOOD AND ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION- A DEVELOPING COUNTRY EXPERIENCE

Pratibha SINGHI<sup>1)</sup>, <u>Arushi Gahlot SAINI<sup>1)</sup></u>, Naveen SANKHYAN<sup>1)</sup>, Jitendra Kumar SAHU<sup>1)</sup>, Sameer VYAS<sup>2)</sup>

<sup>1)</sup> Pedistric Neurology and Neurodevelopmental Unit, Department of Pediatrics

<sup>2)</sup> Department of Radiodiagnosis, Postgraduate Institute of Medical Education and Research, Chandigarh-160012, India

**Objectives**: Acute necrotizing encephalopathy of childhood (ANEC) and acute encephalopathy with biphasic seizures/reduced diffusion (AESD) are two newly described encephalopathy syndromes with characteristic magnetic resonance imaging findings.

**Methods**: We describe the clinico-radiological characteristics and response to treatment in 11 children with these encephalopathy/encephalitis syndromes from North India. We collected retrospective data from patients' case-sheets and prospectively followed them in our neurodevelopmental clinic

**Results**: Among children with AESD (N=7), age of presentation was 1-11 years. All patients showed characteristic, bilaterally symmetrical, diffuse diffusion restriction involving periventricular and subcortical white-matter by day 4 of illness; one patient had occipital dominant pattern of diffusion restriction involving bilateral optic radiations. Cerebrospinal-fluid examination and metabolic screening was normal. Pulse methylprednisolone was administered to all the children. Duration of hospitalization was 7-14 days. Six of the seven patients have normal psychomotor development and neurological examination in follow-up; one case suffered premorbidly from cerebral palsy and has returned back to his pre-illness neurodevelopmental status.

Among children with ANE (N=4), all patients presented with encephalopathy and low Glasgow Coma Scale. Magnetic-resonance-imaging of the brain showed T1 hypointense and T2/FLAIR hyperintense, asymmetrical lesions in bilateral thalami with variable involvement of the brain stem and absence of post-contrast enhancement in all 4 patients. Raised cerebrospinal fluid proteins, serum aminotransferases and hyponateremia were noted. Pulse methylprednisolone was administered to all these children. On the follow-up images, gliotic areas were seen in the thalami. All four children survived; mild to severe neurological deficits persisted in all of them.

**Conclusion**: It is important to recognize ANE and AESD by the characteristic clinical course and MRI, especially in Asian children. Early diagnosis is essential for initiation of timely treatment.

### G-21 EFFICACY AND CNS DEPRESSION OF SECOND-LINE TREATMENT IN CHILDREN WITH FEBRILE STATUS EPILEPTICUS

<u>Masahiro NISHIYAMA<sup>1), 2)</sup></u>, Hiroaki NAGASE<sup>1)</sup>, Yusuke ISHIDA<sup>2)</sup>, Tsukasa TANAKA<sup>2)</sup>, Kyoko FUJITA<sup>2)</sup>, Daisaku TOYOSHIMA<sup>2)</sup>, Azusa MARUYAMA<sup>2)</sup>, Masaaki MATSUMOTO<sup>1)</sup>, Kazumi TOMIOKA<sup>1)</sup>, Ai UNZAKI<sup>1)</sup>, Hiroyuki AWANO<sup>1)</sup>, Hiroki TAKEDA<sup>3)</sup>, Yoshiyuki UETANI<sup>3)</sup>, Satoshi TAKADA<sup>4)</sup>, and Kazumoto IIJIMA<sup>1)</sup>

- <sup>1)</sup> Department of Pediatrics, Kobe University Graduate School of Medicine, Kobe, Japan
- <sup>2)</sup> Department of Neurology, Hyogo Prefectural Kobe Children's Hospital, Kobe, Japan
- <sup>3)</sup> Department of Emergency and Critical Care Medicine, Hyogo Prefectural Kobe Children's Hospital, Kobe, Japan
- <sup>4)</sup> Kobe University Graduate School of Health Science, Kobe, Japan

**Objectives:** Fosphenytoin (fPHT) or continuous midazolam (cMDL) are commonly used as second-line treatment for pediatric status epilepticus (SE) in Japan, but the comparative study of each drug is not available. The objective of this study was to investigate the efficacy and central nervous system (CNS) depression of fPHT and cMDL for pediatric febrile SE (FSE).

**Methods:** The subjects consisted of a retrospective (2002-2009) and prospective (2010-2015) cohort. We included patients who: 1) were admitted to the pediatric intensive care unit at Kobe Children's Hospital because of convulsion or impaired consciousness with fever, 2) were from 1 month to 15 years of age, 3) were injected with either fPHT or cMDL after benzodiazepine administration. We excluded patients who were given two or more second-line treatments defined as injections of fPHT, cMDL, phenytoin, or phenobarbital. Endpoints consisted of the use of barbiturate coma therapy as third-line treatment representing failure of second-line treatment, and full recovery of consciousness at 6 hours after initial neurologic symptoms. We compared characteristics and endpoints between groups of fPHT and cMDL.

**Results:** The number of patients in the group of fPHT and cMDL was 45 and 97, respectively. Characteristics including age, sex, neurological history, body temperature on admission, and duration of convulsion were not significantly different. The rate of barbiturate coma therapy was not different between groups (fPHT: 44%, cMDL: 34%, p = 0.27). The full recovery of consciousness at 6 hours was more frequent in the group of fPHT than cMDL (36% vs. 18%, p = 0.03).

**Conclusions:** This comparative study regarding second-line treatment for FSE indicated that fPHT showed less CNS depression than cMDL. The results suggested that fPHT might be more useful than cMDL in pediatric FSE because drug-induced CNS depression leads to difficulty in distinguishing acute encephalopathy from other conditions.

**G-2** 

#### COMBINATION OF BUMETANIDE, AN ANTAGONIST OF NKCC1, WITH BENZODIAZEPINES CAN RESCUE THE SEQUELAE OF STATUS EPILEPTICUS OF CHILDHOOD

#### Keisuke NAKAJIMA, Haruo OKADO

Department of brain development and neural regeneration, Neural development project, Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan

**Introduction:** Since benzodiazepines (BZPs) became clinically available for the treatment of status epilepticus (SE) in children, the incidence of neurological sequelae has increased in Japan. We hypothesized that the BZPs such as midazolam (MDL) exacerbated sequelae after SE. BZPs strengthen the effect of GABA via increase of the Cl<sup>-</sup> channel opening frequency. The intracellular Cl<sup>-</sup> concentration of neurons is arranged by the balance of NKCC1 and KCC2 co-transporters. When the intracellular Cl<sup>-</sup> concentration increased by high NKCC1/KCC2 ratio with immaturity and/or brain injury, GABA may enhance synaptic excitability. We examined the effect of MDL, against the sequelae using the model of inflammation-induced SE (miSE). Also, we try to use NKCC1 antagonist bumetanide (BUM) in combination with MDL, to inhibit the abnormal excitation.

**Methods:** In postnatal day15 mice, seizure by pilocarpine (PILO) combined with inflammation by Lipopolysaccharide (LPS) was induced. Histological and behavior analysis were performed to evaluate sequelae.

**Results:** Since the combination of LPS and PILO induced specific abnormal behavior and histology, we regard the protocol as suitable for miSE. Next, MDL treatment could rescue some phenotypes, but not rescue the increased apoptosis and the abnormal enhancement of fear contextual memory. Interestingly, the MDL treatment newly induced the immediate early gene (*c-fos*) positive cells at P40, suggesting that MDL treatment exacerbated SE-associated conditions. Moreover, NKCC1/KCC2 ratio of miSE increased at P17. Finally, the combination of BUM with MDL mostly rescued the behavioral and histological phenotypes.

**Conclusions:** It is suggested that the abnormal excitatory GABA transmission induced by MDL in miSE causes the ineffective and inadequate effects of MDL treatment. Since MDL may fail to reduce the sequelae of SE, we will warn about the BZPs single treatment for SE in young age. We propose the effectiveness of the combination of BZPs and BUM for the medication of child SE.

## G-23 SEIZURE REMISSION ON PERAMPANEL IN SIALIDOSIS WITH PROGRESSIVE MYOCLONIC EPILEPSY

Kun-Long HUNG<sup>1), 2)</sup>, Su-Jin HSU<sup>1)</sup>, Hui-Ju CHEN<sup>1)</sup>

<sup>1)</sup> Department of Pediatrics, Cathay-General Hospital, Taipei, Taiwan

<sup>2)</sup> School of Medicine, Fu-Jen Catholic University, New Taipei, Taiwan

**Objectives:** To report the effect of add-on therapy with perampanel in sialidosis with progressive myoclonic epilepsy.

**Case report:** we report on a 15-year-old male patient who suffered from frequent myoclonic seizures for 3 years. Generalized or focal tonic-clonic seizures were sometimes associated. Progressive ataxia, tremor, psychomotor and speech regression developed later. When he was brought to our hospital, he had nearly continuous partial myoclonic seizures in status and kept with 4 anticonvulsants as phenobarbital, sodium valproate, levetiracetam and clobazam in full doses. EEG showed focal spikes arising from C3 and C4. We tried ketogenic diet initially, but seizures progressed to GTCs. Then perampanel were switched on. Adjunctive therapy was started from 4mg/day and titrated to 10 mg/day. Remission of myoclonus and GTCs were achieved, for a follow-up of 6 months. Neurological and cognitive improvements were found gradually. Subsequently, sialidosis was confirmed by the identification of NEU1 gene mutation.

**Conclusions:** Perampanel has been reported as the potential effective treatment for progressive myoclonic epilepsy such as Lafora disease. This is the first report to be also effective for sialidosis.

#### FACTORS ASSOCIATED WITH INTRACTABLE EPILEPSY AFTER CHILDHOOD ACUTE ENCEPHALOPATHY: A RETROSPECTIVE STUDY OF 74 CASES

<u>Yusuke TAKEZAWA</u><sup>1)</sup>, Mai ANZAI<sup>1)</sup>, Wakaba ENDO<sup>1)</sup>, Takehiko INUI<sup>1)</sup>, Taro KITAMURA<sup>2)</sup>, Masaru TAKAYANAGI<sup>2)</sup>, Ikuko SHIRAI<sup>3)</sup>, and Kazuhiro HAGINOYA<sup>1)</sup>

- <sup>1)</sup> Department of Pediatric Neurology, Takuto rehabilitation center for children, Miyagi Children's Hospital, Sendai, Japan
- <sup>2)</sup> Department of Pediatrics, Sendai City Hospital, Sendai, Japan
- <sup>3)</sup> Department of Pediatric Neurology, Tokyo Metropolitan Neurological Hospital, Tokyo, Japan

**Objective:** To describe and analyze etiologies, clinical presentations, treatment and long-term outcomes of intractable epilepsy after childhood acute encephalopathy and identify possible prognostic factors.

**Methods:** We conducted a retrospective review of patients who were diagnosed with acute encephalopathy and had undergone rehabilitation at Takuto Rehabilitation Center for Children between January 2005 and December 2015. Multivariate logistic regression analysis was used to analyze factors associated with intractable epilepsy.

**Results:** We identified 74 patients (32 [43.2%] men and 42 [56.8%] women) with a median onset age of 19 months (range 0.5–111). The types of encephalopathy included AESD (n = 29, 39.2%), HHES (n = 12, 16.2%), and others (n = 33, 44.6%). On multivariate regression analysis, the following factors were independently associated with intractable epilepsy: diagnosis of epilepsy preceding acute encephalopathy [odds ratio (OR) 12.9, 95% confidence interval (95% CI) 1.91–86.7] and usage of more than three anti-epileptic drugs at acute stage of encephalopathy (OR 6.61, 95% CI 1.53–28.5).

**Conclusion:** Diagnosis of epilepsy preceding acute encephalopathy and usage of more than three anti-epileptic drugs at acute stage of encephalopathy may be risks of intractable epilepsy after acute encephalopathy. In contrast, the etiology and type of encephalopathy, treatment and neurodevelopmental retardation preceding acute encephalopathy were not associated with intractable epilepsy.

#### G-25 WHERE EEG UNRAVELS THE ENCEPHALOPATHY: EPILEPSY WITH CONTINUOUS SPIKES AND WAVES DURING SLOW-WAVE SLEEP IN INDIAN CHILDREN

Pratibha SINGHI<sup>1)</sup>, <u>Arushi Gahlot SAINI</u><sup>1)</sup>, Naveen SANKHYAN<sup>1)</sup>, Prahbhjot MALHI<sup>1)</sup>, Niranjan KHANDELWAL<sup>2)</sup>

<sup>1)</sup> Pediatric Neurology and Neurodevelopmental Unit, Department of Pediatrics

<sup>2)</sup> Department of Radiodiagnosis, Postgraduate Institute of Medical Education and Research, Chandigarh-160012, India

**Objectives:** Continuous spikes-and-waves during slow-wave sleep epilepsy (CSWS) is an important epileptic encephalopathy commonly under-diagnosed in young children. It is important to identify CSWS in children presenting with recent-onset cognitive decline or behavioural abnormalities. Data on this epileptic encephalopathy from developing countries is limited.

**Methods:** We analysed the electro-clinical, radiological characteristics, treatment and short-term prognosis of 36 children (age-group 1-14 years) who presented with electrical-status-epilepticus covering >85% of non-REM sleep on electroencephalography.

**Results:** Mean age at presentation was 6.2+1.9 (range 3.25-14 years); majority (75%) were boys. Most common parental concerns were seizures (100%), poor school performance (86%), behavioural problems (74%) and developmental delay (47%). First neurological symptom was seizure (50%) or developmental delay (41%). Seizures were focal (62%), generalized (59%), atypical-absences (41%) and atonic (24%) type. Mean age at clinical deterioration was 4.8+2 years; at detection of electrical status epilepticus was 6.3+2 years. Magnetic-resonance-imaging showed normal scan (25%); polymicrogyria/ pachymicrogyria (22%), old intracranial-bleed (8%), hypoglycaemic insult (5.5%), hypoxic-ischemic changes (2.7%), hydrocephalus (2.7%) and miscellaneous non-specific changes (33%). Final aetiology was structural 48%, idiopathic 19% and unknown 33%. Mean duration of follow-up was 26+17.5 months. Pulse-corticosteroid was administered in 80%; electrical status epilepticus persisted in 43% patients. Vineland-social-maturityscale was available in 64%; mental-retardation was moderate in 29%; severe, mild and border-line each in 15%; profound, low-average and average each in 10%. Seizures, behavioural, cognitive and scholastic problems persisted in 43%, 46%, 49% and 57% of cases respectively.

**Conclusions:** This is the largest clinical series of CSWS from India. Our study highlights that CSWS should be considered in children with polymorphic seizures and new/recent-onset behavioural or cognitive; significant proportions have residual neurological problems at short term follow-up.

### FEBRILE INFECTION- RELATED EPILEPSY SYNDROME (FIRES): A CASE REPORT

#### <u>Allyn Nicole LIM</u>, Martha LU-BOLANOS Philippine General Hospital, Manila, Philippines

**Objectives:** 1) To present a possible case of febrile infection-related epilepsy syndrome (FIRES). 2) To give an overview about FIRES with regards to its history, clinical course, pathogenesis, management and outcome.

**Introduction:** Febrile infection-related epilepsy syndrome is an explosive onset, potentially fatal acute encephalopathy following an acute febrile illness.

**Case:** This is a case of an 8 year old female who presented with status epilepticus after a bout of urinary tract infection. Work up for bacterial and viral infection was negative. CSF sent abroad turned out to be negative for all autoimmune antibodies included in their panel. Anti- epileptic drugs were started and maximized. Patient was also started on propofol, however developed kidney injury hence it was discontinued. Ketamine was started thereafter. On discharge, patient was seizure free and functioning well, with mild cognitive impairment.

**Discussion:** FIRES has an incidence of 1:1,000,000 and develops in children aged 3-15. Viral infections usually precede the syndrome with the respiratory tract as the most common source. The fever of FIRES is typically biphasic, with a seizure-free period between the resolution of fever and the onset of symptoms ranging from 2 to 14 days. Thereafter, the acute period of the disease develops, lasting from 1 to 12 weeks. A febrile illness preceding the convulsions would likely point to an infectious encephalitis. Initial magnetic resonance imaging is normal in half of the patients. Treatment modalities that show promising results include lidocaine or anesthetics and immunomodulators. Another treatment that shows promising results is the ketogenic. The mortality rate of FIRES is as high as 30%. In children, intellectual disability with physical and behavioral disturbance was seen in the survivors.

**Keywords:** febrile infection- related epilepsy syndrome, encephalitis, ketamine, status epilepticus



## G-27 TWO CASES OF ACUTE ENCEPHALITIS WITH REFRACTORY, REPETITIVE PARTIAL SEIZURES TREATED WITH LEVETIRACETAM

<u>Kaori MIZUKAWA</u><sup>1), 2)</sup>, Kanako MARUTA<sup>1), 3)</sup>, Kunihiro MATUNAMI<sup>1)</sup>, Atsushi IMAMURA<sup>1)</sup>

<sup>1)</sup> Department of Pediatrics, Gifu Prefectural General Medical Center, Gifu, Japan

<sup>2)</sup> Department of Pediatrics, Ichinomiyanishi Hospital, Ichinomiya, Japan

<sup>3)</sup> Department of Pediatrics, Nagara Medical Center, Gifu, Japan

Acute encephalitis with refractory, repetitive partial seizures (AERRPS) is a new epileptic syndrome described by Sakuma in Japan in 2001. Now, we have experienced two cases of AERRPS treated with levetiracetam (LEV).

Patient 1 was a 10-year-old boy. On 3 days from the onset, he had intractable seizure, which was not able to be suppressed by intravenous thiamylal and oral VPA. However, it was controlled after LEV added on. His seizure recurred after tapering off thiamylal and administration with phenobarbital (PB). However, it was also suppressed after LEV increased to 1500 mg (50 mg/kg). On 49 days from the onset, he could get out of artificial ventilator. Patient 2 was a 10-year-old boy. His intractable seizure was suppressed by intravenous thiamylal. Anti-epilepsy-drugs (AEDs) were gradually replaced by oral PB and LEV, and he could get out of artificial ventilator on 36 days from the onset. However the seizure recurred after tapering with PB, it was disappeared after LEV increased to 2250 mg (56.2 mg/kg).

AERRPS has prodromal, aggravation, acme, convalescence, and chronic stage. The patients with AERRPS often suffer from relapse of seizure during the transition from thiamylal to alternative AEDs in convalescence phase. We have experienced LEV effective cases with the transition from intravenous thiamylal to oral AEDs. LEV may be one of the alternative AEDs in the recovery period of AERRPS.

#### AUTOANTIBODY AS A FAVORABLE PROGNOSTIC MARKER ~MYELIN-OLIGODENDROCYTE GLYCOPROTEIN ANTIBODIES IN JAPANESE PEDIATRICS WITH ACUTE DISSEMINATED ENCEPHALOMYELITIS~



<u>Naomi HINO-FUKUYO</u><sup>1), 2)</sup>, Kazuhiro HAGINOYA<sup>2)</sup>, Ichiro NAKASHIMA<sup>3)</sup>, Douglas Kazutoshi SATO<sup>3)</sup>, Toshiyuki TAKAHASHI<sup>3)</sup>, Tatsuro MISU<sup>3)</sup>, Kazuo FUJIHARA<sup>3)</sup>, Shigeo KURE<sup>2)</sup>

<sup>1)</sup> Center of Genomic Medicine, Tohoku University Hospital, Sendai, Japan

<sup>2)</sup> Department of Pediatrics, Tohoku University School of Medicine, Sendai, Japan

<sup>3)</sup> Department of Neurology, Tohoku University of School of Medicine, Sendai, Japan

**Background:** High titers of anti- myelinating oligodendrocyte glycoprotein (MOG) antibodies have been detected in a subgroup of pediatric diseases such as acute disseminated encephalomyelitis (ADEM). MOG and aquaporin-4 (AQP4) have been extensively analyzed as targets for humoral immune reactions in central nervous system (CNS) demyelinating diseases, and the results indicated a possible role of these antibodies in the pathogenesis of various demyelinating diseases. However, no such studies have been conducted in pediatric patients with inflammatory CNS disorders in Japan.

**Objective:** To investigate the antibody titer levels against MOG and AQP4 in pediatric patients with inflammatory CNS disorders, and to evaluate clinical significance to study anti-MOG antibodies.

**Methods:** Sera at onset from patients with acute disseminated encephalomyelitis (ADEM) in 7, optic neuritis (ON) in 5, pediatric multiple sclerosis (MS) in 4 and neuromyelitis optica in one were tested for MOG and AQP4 antibodies using cell-based assays with live transfected cells. The duration of the observation periods ranged from one to twenty one years (median, ten years). Clinical courses were also assessed in the patients with positive anti-MOG antibodies.

**Results:** Among 17 patients diagnosed with inflammatory CNS demyelinating diseases nine (52%) were positive to anti-MOG antibodies. Of note, all cases with positive anti-MOG antibodies showed seronegativity against anti-AQP4 antibodies and had a favorable prognosis. In our study, no patient with positive anti-MOG antibodies has poor prognosis, although some patients has been relapsed.

**Conclusions:** The positivity against MOG-Ab may indicate a favorable prognosis in inflammatory CNS disorders (ADEM, ON, and MS). This preliminary report showed that anti-MOG antibodies testing at onset could be a useful tool predicting clinical outcome of children with ADEM.

#### G-29 THERAPEUTIC RESPONSE TO PULSED INTRAVENOUS METHYL PREDNISOLONE IN PAEDIATRIC ANTI-N-METHYL-D-ASPARTATE-RECEPTOR ENCEPHALITIS (NMDARE)

<u>Bindu Parayil SANKARAN</u><sup>1)</sup>, Madhu NAGAPPA<sup>1)</sup>, Anita MAHADEVAN<sup>2)</sup>, Mathuranath PS<sup>1)</sup>, Sanjib SINHA<sup>1)</sup>, Arun B TALY<sup>1)</sup>

<sup>1)</sup> Depts of Neurology, National Institute of Mental Health And Neurosciences, Bangalore, India

<sup>2)</sup> Department of Neuropathology, National Institute of Mental Health & Neurosciences, Bangalore, India.

**Background:** Experience on optimal nature & duration of immunosuppressive therapy in peadiatric anti NMDAR is limited. We hypothesized that pulsed methyl prednisolone is effective in inducing & maintaining remission in this autoimmune disorder of childhood similar to other immune-mediated disorders of nervous system viz myasthenia gravis, vasculitis

**Methods:** This prospective, hospital-based, longitudinal study was carried out between July 2012 to November 2015. Inclusion Criteria were 1) Children < 18 years 2) Monophasic/ Relapsing-Remitting Neuropsychiatric illness 3) Anti-NMDAR antibodies in serum/ cerebrospinal fluid by indirect immunofluorescence

**Results:** Twenty children (boys=3; mean age=10.25+4.7years) with anti-NMDAR encephalitis were identified during the study period. Mean duration of index episode was 36.9±28.5days (range: 3-127days). Five had antecedent fever and four had previous episodes of neuropsychiatric illness. Abnormal behaviour, global regression, hyperkinetic movements and seizures were universal. Salient lab observations were: abnormal EEG (20/20), abnormal brain MRI (3/20) and CSF pleocytosis (2/19). All received MP (30mg/kg/day, intravenous infusion, for five days) during the acute phase. Plasmapheresis (n=11) or intravenous immunoglobulin (n=4) were given when symptoms were severe and therapeutic response was suboptimal. Subsequently, monthly MP was administered to maintain remission. Nineteen patients were followed up for a mean duration of 16.68+9.5months (range: 4–39months). Three had recurrence of partial syndrome, related to delay in pulsed MP. They maintained improvement with re-initiation of pulsed MP. All recovered significantly from encephalopathy and were able to resume schooling. Pre-treatment modified Rankin Score was five, which improved to 0 or 1 in 18 children followed-up for greater than 6 months.

**Conclusion**: We highlight the beneficial effects of pulsed MP in paediatric anti-NMDARE. Intravenous pulsed MP is effective in inducing and maintaining remission and obviates the need for more toxic and expensive agents.

#### ANTI-HU ANTIBODY ASSOCIATED NEUROLOGICAL DISEASE, PRESENTING WITH HEMISPHERIC ENCEPHALOPATHY AND INTRACTABLE EPILEPSY IN CHILDREN

#### Masanori TAKEOKA

Division of Epilepsy and Clinical Neurophysiology, Department of Neurology, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts, USA

**Objective:** Anti-Hu antibodies (ANNA-1: anti-neuronal nuclear antibodies, type I) are commonly associated with paraneoplastic encephalomyelitis in adults, typically with small cell lung cancer. Anti-Hu antibodies are extremely rare in children, seen in cases of neuroblastoma with or without associated opsoclonus-myoclonus syndrome, or with limbic encephalitis without associated malignancy. We present a 5 year old girl with hemispheric encephalopathy and intractable epilepsy, with clinical features of Rasmussen's encephalitis.

**Methods:** The patient had semi-acute onset of focal motor seizures at 4 years of age, consisting of right face and arm clonic movements lasting one minute, seen up to five times a day. She developed progressive right facial weakness. EEG showed left hemispheric slowing and with left fronto-temporal predominant focal seizures. Subsequent serial brain MRI studies showed progressive left hemispheric atrophy and T2 signal hyperintensity in the left frontal lobe, insula and left caudate head. She had no evidence of developmental delay or regression.

Results: Diagnostic evaluation revealed serum anti-Hu antibody titer of 1:960 (normal <1:240), CSF anti-Hu antibody titer of 1:16 (normal <1:2), 13 CSF oligoclonal bands, and CSF neopterin 67 nmol/L (normal 7-40). Serum striational antibody titer was 1:3840 (normal <1:120) and serum TPO antibody was mildly elevated at 15.6 IU/mL (normal <15), which appeared to be non-specific. MR angiogram of the head and diagnostic workup for an associated malignancy including whole body MRI were unremarkable. She was started on immunosuppressive treatment with cyclophosphamide and methylprednisone, followed by mycophenolate mofetil, and she has had decreased seizures.

Conclusion: This is a very unique case of anti-Hu antibody associated encephalopathy with features of Rasmussen's Encephalitis, in a child without evidence of a primary malignancy. This case provides insights into the spectrum of neurological disorders associated with anti-Hu antibodies, including new-onset intractable focal seizures and focal encephalopathy, even with features of Rasmussen's encephalitis.

#### G-31 CHRONIC ENCEPHALITIS ASSOCIATED WITH ANTI-MYELIN OLIGODENDROCYTE GLYCOPROTEIN ANTIBODIES

<u>Hiroya NISHIDA</u><sup>1)</sup>, Asami ITO<sup>2)</sup>, Satoko KUMADA<sup>1)</sup>, Sunao TOMITA<sup>2)</sup>, Kimihiko KANEKO<sup>3)</sup>, Hiroshi SAKUMA<sup>4)</sup>, Yasuhiro NAKATA<sup>5)</sup>, Mayumi KUBOTA<sup>6)</sup>, Toshiyuki TAKAHASHI<sup>3)</sup>, Ichiro NAKASHIMA<sup>3)</sup>, Makoto TANIGUCHI<sup>6)</sup>, Tetsuharu KAMIOKA<sup>1)</sup>, Tomoko MIZUNO<sup>1)</sup>, Shumpei UCHINO<sup>1)</sup>, Eiji KURIHARA<sup>1)</sup>, Takashi KOMORI<sup>7)</sup>

- <sup>1)</sup> Department of Neuropediatrics, Tokyo Metropolitan Neurological Hospital, Tokyo, Japan
- <sup>2)</sup> Department of Neurology, Tokyo Metropolitan Children's Medical Center, Tokyo, Japan
- <sup>3)</sup> Department of Multiple Sclerosis Therapeutics, Tohoku University, Graduate School of Medicine, Miyagi, Japan
- <sup>4)</sup> Developmental Neuroimmunology Project, Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan
- <sup>5)</sup> Department of Neuroradiology, Tokyo Metropolitan Neurological Hospital, Tokyo, Japan
- <sup>6)</sup> Department of Neurosurgery, Tokyo Metropolitan Neurological Hospital, Tokyo, Japan
- <sup>7)</sup> Department of Neuropathology, Tokyo Metropolitan Neurological Hospital, Tokyo, Japan

**Objective:** To present the unique clinical and neuropathological features of a patient with chronic encephalitis associated with serum anti-myelin oligodendrocyte glycoprotein (MOG) antibodies.

Case presentation: A 16-year old woman was admitted to our hospital because of psychomotor regression. She had epileptic seizures since age 8 years, and was diagnosed with attention deficit/hyperactivity disorder at age 10 years. Psychiatric symptoms were aggravated from age 13 years, and her mental status deteriorated from age 14 years. She developed progressive spastic quadriplegia from age 16 years. There was no history of optic neuritis. On admission, she was bedridden and did not comprehend simple commands. Although she could follow objects, right homonymous hemianopsia was suspected. She showed swallowing disturbance. Blood and cerebrospinal fluid examinations revealed no abnormalities, except for a high titer of serum anti-MOG antibodies detected by highly specific cell-based assay (CBA). Brain magnetic resonance imaging (MRI) showed extensive white matter lesions with multiple ring-like enhancement. Lesions in the thalamus and brainstem were also observed. Follow-up MRI showed that distribution of the lesions as well as enhanced structures changed at short intervals. Spinal MRI revealed no abnormalities. Brain biopsy was conducted to rule out granulomatous and neoplastic disorders, and revealed inflammatory white matter damage with T-cell infiltration. Methylprednisolone pulse therapy has just been started.

**Conclusion:** Anti-MOG antibodies are associated with several inflammatory neurological diseases, including monophasic and multiphasic acute disseminated encephalomyelitis, optic neuritis, and neuromyelitis optica. The unique clinicopathological presentation of our patient may broaden the clinical spectrum of anti-MOG-antibody-associated neurological disorders.

OP-0'

### HIGH MOBILITY GROUP BOX 1 ENHANCED ACQUIRED EPILEPSY IN A RODENT MODEL OF INFANTILE FEBRILE STATUS EPILEPTICUS

<u>Masanori ITO</u><sup>1)</sup>, Mitsumasa FUKUDA<sup>1)</sup>, Hajime YANO<sup>2)</sup>, Hisaaki TAKAHASHI<sup>2)</sup>, Yoshiaki YANO<sup>2)</sup>, Junya TANAKA<sup>2)</sup>, and Eiichi ISHII<sup>1)</sup>

<sup>1)</sup> Department of Pediatrics, Ehime University Graduate School of Medicine, Toon, Ehime, Japan

<sup>2)</sup> Department of Molecular and Cellular Physiology, Ehime University Graduate School of Medicine, Toon, Ehime, Japan

**Objectives:** Resent study reported that the high mobility group box 1 (HMGB1), an important inflammatory mediator, were related the pathogenesis of febrile seizure (FS). Here we investigated the role of HMGB1 in acquired epilepsy using prolonged hyperthermia-induced seizures (pHS) in immature rats, a model of human febrile status epilepticus.

**Method:** On postnatal day (P) 10, male Lewis rats were divided into pHS + HMGB1 (n = 15) and pHS (n = 20) groups. We intranasally applied HMGB1 24 h after pHS. Passive avoidance and rotarod tests were performed on P80. EEG electrodes were implanted on P85, and EEGs were recorded for 24 h on P90 and P120. Histological analysis was performed on P150.

**Results:** Spontaneous seizure incidence in the pHS + HMGB1 group was significantly higher than that in the pHS group (P = 0.027). There was no significant difference between these groups for the passive avoidance and rotarod tests. Histological analysis showed that astrocytes were significantly increased in CA1, CA3, and the corpus callosum in the pHS + HMGB1 with epilepsy group (n = 6) than that in the pHS + HMGB1 without epilepsy group (n = 9). There was no significant difference between these two groups for either neuronal or oligodendrocyte cell counts.

**Conclusion:** Constitutive activity of HMGB1 has been shown to activate N-methyl-Daspartate (NMDA) receptors via toll-like receptor 4, and NMDA receptor function is believed to play an important role in the pathogenesis of both ictogenesis and acquired epileptogenesis. Our results indicate that infantile febrile status epilepticus with HMGB1 overproduction may predispose to adulthood epileptogenesis and to the development of secondary epilepsy. Further, astrogliosis also have played an important role in acquired epileptogenesis in our model. Future studies using cultured cells are required to clarify the mechanism by which HMGB1 contributes to acquired epileptogenesis.

#### OP-02 NGS-BASED EPILEPSY GENE PANEL TEST IN EARLY-ONSET CHILDHOOD EPILEPSY

<u>Jiwon LEE<sup>1</sup></u>, Chung LEE<sup>2), 3)</sup>, Nayoung K. D. KIM<sup>2)</sup>, Jeehun LEE<sup>1)</sup>, Chang-Seok KI<sup>4)</sup>, Woong-Yang PARK<sup>2), 3), 5)</sup>, and Munhyang LEE<sup>1)</sup>

- <sup>1)</sup> Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea
- <sup>2)</sup> Samsung Genome Institute, Samsung Medical Center, Seoul, Korea
- <sup>3)</sup> Department of Health Sciences and Technology, SAIHST, Samsung Medical Center, Seoul, Korea
- <sup>4)</sup> Department of Laboratory Medicine and Genetics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea
- <sup>5)</sup> Department of Molecular Cell Biology, Samsung Medical Center, Seoul, Korea

**Objectives:** The genetic causes of epilepsy are presumed to be multifactorial and are important in childhood epilepsy. Recent studies revealed that various genetic mutations linked to genetic epileptic syndromes and provided information about the mechanism of epileptogenesis, prognosis, and adequate treatment. In this study, we try to detect genetic mutations through epilepsy gene panel using next generation sequencing (NGS) in early-onset epilepsies in childhood.

**Methods:** We retrospectively reviewed the medical records of 33 patients (female : male = 18 : 15) with early-onset ( $\leq 2yr$ ) epilepsy at Samsung Medical Center between June 2014 and July 2015. The patients with symptomatic etiologies such as structural brain lesions were excluded. We designed customized NGS-based epilepsy gene panel containing total 111 genes which included 38 candidate genes for genetic generalized epilepsy syndromes and 73 genes for other genetic epilepsy. The gene panel included the coding exons, and intro-exon boundaries using bidirectional sequencing.

**Results:** The mean age of seizure onset was  $0.8 \pm 0.55$  years (range, 3 days to 2 years old). Nineteen patients (57.6%) had severe developmental delay and three had psychiatric disorders. One sibling case was included and 14 patients had a family history of epilepsy (n = 8) or febrile seizure (n = 8). In 12 patients (36.4%), we identified mutations which were known to be associated with genetic epilepsy disorders: *SCN1A* (n = 6, 50%), *SCN8A*, *PCDH19*, *PRRT2* (n = 2, 16.7%), *ARX*, *KCNQ2*, and *FOXG1*. In five children with presumed as Dravet syndrome clinically, four were confirmed to have a *SCN1A* mutation and the other one had a *PCDH19* mutation. One family was revealed to have *PRRT2* mutation. Six patients with mutation were sporadic cases without family history.

**Conclusions:** Our data demonstrated the clinical efficacy of NGS-based epilepsy gene panel for screening in not only patients with clinically suspicious of specific syndrome but also sporadic cases. NGS-based epilepsy gene panel makes another step forward in diagnosis and new therapeutic approaches of childhood intractable epilepsy.

OP-03

### DRAVET SYNDROME PRESENTING AS WEST SYNDROME SECONDARY TO SCN1A MUTATION- A RARE REPORT OF TWO CASES

<u>Vykuntaraju K. GOWDA<sup>1</sup></u>, Varun RAGHAVAN<sup>2</sup>, Naveen BENAKAPPA<sup>3</sup>, Asha BENAKAPPA<sup>3</sup>

<sup>1)</sup> Assistant Prof of Pediatric Neurology, Indira Gandhi institute of child health, Bangalore, India

<sup>2)</sup> Bangalore medical college and research institute, Bangalore, India

<sup>3)</sup> Prof of Pediatrics, Indira Gandhi institute of child health, Bangalore, India

**Objective:** To report two rare cases of Dravet syndrome presenting with infantile spasms secondary to a Mutation in SCN1A gene

**Methods:** Retrospective chart review of two cases of west syndrome with Dravet syndrome.

**Results:** Case 1 is a 13 month old boy with developmental delay and infantile spasms. First episode of seizures following 3rd dose of DPT vaccination. On examination he had microcephaly (39 cm), spasticity of all four limbs. EEG was suggestive of hypsarrythmias and MRI of brain was normal. Genetic testing revealed a homozygous missense variant (c.3199G>A;p.Ala1067Thr) in Exon 16 of SCN1A gene. The patient responded for vigabatrine. Case 2 is a 35 month male patient with normal birth and family history presented with mild developmental delay and history of fever triggered seizures in the form of GTCS after which he started developing infantile spasms in clusters. Examination revealed a head size of 49 cm with normal tone. EEG was suggestive of hypsarrythmias with normal MRI of brain. Genetic analysis revealed a homozygous missense variant (c.3199G>A;p.Ala1067Thr) in Exon 8 of SCN1A gene. The patient's seizures have reduced steroids.

**Conclusion:** Dravet syndrome should be considered in the differential diagnosis of west syndrome in addition to other causes described.

#### OP-04 ELECTROENCEPHALOGRARHY FINDINGS TO PREDICT ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION

<u>Atsuko OHNO</u><sup>1)</sup>, Akihisa OKUMURA<sup>2)</sup>, Tatsuya FUKASAWA<sup>3)</sup>, Takeshi SUZUKI<sup>3)</sup>, Yuji NAKAMURA<sup>4)</sup>, Misa MIYAKE<sup>5)</sup>, Tetsuo KUBOTA<sup>3)</sup>, Takeshi TSUJI<sup>6)</sup>, Naoki ANDO<sup>7)</sup>, Shinji SAITOH<sup>7)</sup>, Jun NATSUME<sup>1)</sup>

<sup>1)</sup> Department of Pediatrics, Nagoya University, Nagoya, Japan

- <sup>2)</sup> Department of Pediatrics, Aichi Medical University, Nagakute, Japan
- <sup>3)</sup> Department of Pediatrics, Anjo Kosei Hospital, Anjo, Japan
- <sup>4)</sup> Department of Pediatrics, Toyohashi municipal hospital, Toyohashi, Japan
- <sup>5)</sup> Department of Pediatrics, Fujita Health University School of Medicine, Toyoake, Japan
- <sup>6)</sup> Department of Pediatrics, Okazaki City Hospital, Okazaki, Japan
- <sup>7)</sup> Department of Pediatrics and Neonatology, Nagoya City University, Nagoya, Japan

**Objective:** It is important to differentiate acute encephalopathy with biphasic seizures and late reduced diffuseon (AESD) from prolonged febrile seizure (PFS) early as possible. To clarify the usefulness of electroencephalogram (EEG) for early differentiation of AESD and PFS, we reviewed EEGs recorded in the early stage of AESD or PFS.

**Methods:** From Tokai Pediatric Neurology Society database between 2009 and 2015, we enrolled 8 patients with AESD and 13 with PFS who underwent EEG within 3 days from the onset. EEGs were evaluated by 2 or more pediatric neurologists. We examined focal or generalized slowing, spindles, fast waves, and paroxysmal discharges.

**Results:** Median age at disease onset was 12 months (range 5-85 months) and 18 months (range 5-137 months) in AESD and PFS groups, respectively. Median date of EEG recording was 2nd from the day of onset in both groups. Focal or generalized slowing was observed in 4 of 8 (50%) patients with AESD, and 5 of 13 (38%) with PFS. Absence of spindles was observed in 8 (100%) patients with AESD and 1 (9%) patient with FPS. Decrease of fast waves was observed in 4 (50%) patients with AESD and none with PFS. Paroxysmal discharges were not observed in any patients. Fisher's exact test revealed that absence of spindle and decrease of fast waves were significantly more frequent in patients with AESD than those with PFS (p<0.01 and p=0.01, respectively).

**Conclusion:** EEG within the first few days from the onset of prolonged seizures will be useful for the differentiation of these disorders. Absence of spindles and decrease of fast waves can be key findings to distinguish AESD from PFS.
OP-05

#### TWO CASES OF ACUTE BRAIN SWELLING-TYPE ENCEPHALOPATHY

<u>Masataka FUKUOKA</u><sup>1)</sup>, Kiyoko AMOU<sup>1)</sup>, Megumi NUKUI<sup>2)</sup>, Ichiro KUKI<sup>2)</sup>, Shin OKAZAKI<sup>2)</sup>, Junichi ISHIKAWA<sup>3)</sup>, Hiroshi RINKA<sup>3)</sup>, Masao TOGAWA<sup>1)</sup>, Hisashi KAWAWAKI<sup>2)</sup>, Masashi SHIOMI<sup>4)</sup>

<sup>1)</sup> Department of Pediatric Emergency, Osaka general city hospital, Osaka, Japan

<sup>2)</sup> Department of Pediatric Neurology, Osaka general city hospital, Osaka, Japan

<sup>3)</sup> Emergency and critical care center, Osaka general city hospital, Osaka, Japan

<sup>4)</sup> Department of Pediatrics, Aizenbashi hospital, Osaka, Japan

**Introduction:** Acute brain swelling (ABS) -type encephalopathy is a life-threatening disease that develops from convulsions and slight consciousness disturbance, and results in brain hernia along with the acute progression of brain edema. Although the cause of brain edema is unknown, as it may be reversible, it is essential for prognosis improvement to avert the progression of brain hernia in the acute phase.

**Case:** We encountered 2 cases of ABS with different prognoses. The first case developed from pyrexia, convulsions, and slight consciousness disturbance. Twelve hours after the first convulsions, the patient experienced respiratory arrest. The pupils were dilated, marked brain edema was noted on CT, and blood sodium was as low as 130 mEq/L (hyponatremia). Following barbiturate therapy, normothermia therapy, anti-brain edema therapy, and immunoregulatory treatment, the patient recovered from ABS without sequelae. The second case developed from pyrexia, vomiting, and cluster convulsions. Hyponatremia was observed (blood sodium: 127 mEq/L), and marked brain edema was noted on CT. Seven hours after the first convulsions, the patient experienced cardiopulmonary arrest, which resulted in clinical brain death. While pneumococcus was identified as the causative agent on blood culture in the first case, the causative agent was unspecified in the second case.

**Discussion:** In both cases, the acute progression of brain edema and hyponatremia occurred within 12 hours after the onset of convulsions. Conversely, the poor prognostic case showed a shorter time from the first convulsions to acute deterioration and more frequent convulsions than the case with a favorable prognosis. In cases of suspected acute encephalopathy, we should assume the disease state of ABS, perform anticonvulsant treatment and correction for hyponatremia, be aware of changes in clinical symptoms and the acute progression of brain edema on CT assessment, and introduce anti-brain edema therapy.

#### OP-06 CLINICAL FEATURES AND CEREBROSPINAL FLUID CYTOKINE PROFILE OF PEDIATRIC ANTI-NMDAR ENCEPHALITIS

<u>Tomonori SUZUKI</u><sup>1), 2)</sup>, Eri NAKAHARA<sup>1), 3)</sup>, Hiroshi SAKUMA<sup>1)</sup>, and Masaharu HAYASHI<sup>1)</sup>

<sup>1)</sup> Developmental Neuroimmunology Project, Department of Brain Development and Neural Regeneration, Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan

<sup>2)</sup> Department of Pediatrics, Tokyo Medical Dental University, Tokyo, Japan

<sup>3)</sup> Department of Pediatrics, Juntendo University, Tokyo, Japan

**Objective:** To report the clinical features and cerebrospinal fluid (CSF) cytokine profile of pediatric patients with anti-N-methyl-D-asprtate receptor (NMDAR) encephalitis

**Patients and Methods:** From 2013 to 2016, we screened antineuronal antibodies in sera and CSFs from 200 pediatric patients (under 18 y.o) with suspected autoimmune or inflammatory neuronal disorders. Antineuronal antibodies (Abs) were tested using immunohistochemistry, immunocytochemistry, and cell-based assay (Euroimmun). Ten patients were positive for anti-NMDAR Ab and were diagnosed as anti-NMDAR encephalitis. Clinical features, laboratory data, neuroradiological findings, and therapies were reviewed, and CSF cytokines were measured by bead based flow cytometric assay.

**Results:** The median age of the patients was 7 years (range, 2-14 years), 90% were female, 20% coexisted with ovary teratoma. Clinical manifestations included psychiatric symptoms in 9 (e.g. agitation and mood instability); movement disorders in 7; seizure in 6; behavioral problems in 7 (e.g. hyperactivity and stereotyped movement); memory deficit in 2. Three patients had autonomic dysfunction but none had central hypoventilation. Patients under 7 years often had movement disorders (100%), seziures (80%, predominantly focal seizure), and speech dysfunction (80%). The mean CSF cell count was  $14.9\pm13.4$  ( $\pm$ SD) /µL, and the mean CSF protein was  $25.1\pm19.2$  ( $\pm$ SD) mg/dL. Electroencephalography was abnormal in 7 patients. Only one patient had abnormal brain image findings. Eight patients were treated methyl-plednisolone pulse therapy, and 7 received intravenous immunogulobulin, and no patient underwent plasma exchange. One patient received rituximab, 2 required artificial ventilation. The CSF levels of CXCL13, CXCL10 and IL-6 were elevated in some patients.

**Conclusions:** Clinical features observed in these patients were nearly identical to those in the reported cases. Patients under 7 years were more likely to have seizure and speech dysfunction. Cytokines and chemokines related to antibody production were occasionally increased in CSF.

#### A CASE OF AERRPS WITH PAHLOGICAL FINIDNGS

<u>Ayuko YOSHIDA</u>, Yuka SUZUKI, Satoshi MANIWA, Youichi KONDOU Department of Pediatrics, Matsuyama Red Cross Hospital, Ehime, Japan

**Objective:** Acute encephalitis with refractory, repetitive partial seizures (AERRPS) is a newly defined encephalitis described by Sakuma in Japan in 2001.We present a boy with severe AERRPS proceeded by typical juvenile myoclonic epilepsy (JME).

Methods: A 14-year-old Japanese boy was presented with repetitive partial seizures.

**Results:** Three years after diagnosed as JME, he started having partial seizures that are compatible with left hemisphere onset, and status epileptics accompanied by high fever. The patient required the continuous intravenous antiepileptic drugs (AED). His MRI and EEG both showed left occipital region at first, however new regions appeared rapidly in left parietal and bilateral frontal area under Methylprednisolone pulse therapy. Proinflammatory cytokine level in his cerebrospinal fluid (CSF) was increased and brain biopsy showed CD34 positive capillary hyperplasia and rarefaction in cortex. IgG antibodies against the glutamate receptor (GlluR) was negative both in CSF and peripheral blood. Based on his clinical course, we diagnosed him as having AERRPS. Over next 10 months, we were unable to discontinue intravenous AED though several immunosuppressive therapies. Due to prolonged bed ridden and sedated status, he developed massive deep vein thrombosis, and we lost him due to septic shock.

**Conclusion:** His serial MRI study showed progressively spreading region, which was atypical findings compared with previous reported cases. Active region in his MRI had relatively old pathological findings without ongoing inflammatory changes.



## OP-08 TREATMENT AND PROGNOSIS ASSOCIATED WITH HUMAN PARECHOVIRUS 3 ENCEPHALITIS WITH A NEONATAL ONSET

<u>Kiyohiro KIM</u>, Hisashi KAWAWAKI, Ichiro KUKI, Masataka FUKUOKA, Yuka HATTORI, Hitomi TSUJI, Megumi NUKUI, Shin OKAZAKI Department of Pediatric Neurology, Osaka City General Hospital, Osaka, Japan

**Introduction:** There have been a number of reports on human parechovirus 3 (HPeV-3) that infected patients' central nervous system during the neonatal period and early infancy and caused marked neurological sequelae. However, few have described the disease state or provided details of the therapeutic approach. In the present report, we report a neonatal case of HPeV-3 infection complicated by right transverse sinus venous thrombosis in addition to a white matter lesion on brain MRI.

**Case:** A 10-day-old male neonate who presented with pyrexia on Day 9 and developed convulsive seizure and central apnea on Day 10. Brain MRI showed bilaterally symmetric, diffuse white matter hyper-intense signals on a diffusion-weighted image. HPeV-3 encephalitis was suspected, and treatment was initiated. Blood examinations revealed coagulation abnormality as well as high ferritin and neopterin. Although cerebrospinal fluid pleocytosis was not noted, fluid neopterin was high. Since HPeV-3 encephalitis was complicated by hypercytokinemia, which may have worsened his clinical condition, dexamethasone was given. The white matter lesion partially revealed cystic changes, but these were mostly resolved, and the patient was discharged from our hospital without neurological abnormal findings on Day 27. On admission, real-time PCR detected HPeV-3 in the blood, spinal fluid, and nasal discharge. Transverse sinus venous thrombosis followed encephalitis, but it disappeared rapidly with anticoagulant treatment. The developmental quotient was 95 points at 1 year, and the patient has not developed epilepsy.

**Conclusion:** In HPeV-3 encephalitis patients who may be complicated by hypercytokinemia, we should consider immunomodulatory treatment, such as corticosteroid administration, in order to inhibit the progression of encephalopathy.

**OP-0**9

### PROGNOSTIC OVERVIEW OF EPILEPTIC ENCEPHALOPATHIES STARTING IN THE INFANTILE PERIOD

<u>Kanako TAKEDA</u>, Miho ADACHI, Hitoshi YAMAMOTO, Yusaku MIYAMOTO, Shuji HASHIMOTO, Hisako YAMAMOTO, Noriko UDAGAWA, Natsuko ARAI, Hiroshi MURAKAMI, Shoutaro KAKU, Taichi IMAIZUMI Department of Pediatrics, St. Marianna University School of Medicine, Kawasaki, Japan

**Purpose:** The epileptic encephalopathy (EE) is defined as seizures are typically difficult to control, seizures are strongly associated with mental retardation, and seizure onset is usually under 2 years old. We evaluated the clinical progress of 10 children with EE in the past three years and discussed the issues related to seizure outcome and psychomotor development.

**Methods:** The subjects are 3 patients with West syndrome, 4 patients with intractable epileptic seizures of unknown etiology and 3 patients with congenital brain anomaly (7 males and 3 females). Developmental quotient (DQ) before and after treatments was also estimated.

**Results:** The mean age of seizure onset is 5.2 ms (SD:  $\pm 4.6$  ms). There were 2 surgical candidates in this study. A range of DQ after the therapy was 20 to 80 in this study. All of the patients required to take more than two anti-epileptic drugs showed progressive mental retardation or deterioration after the seizure onset. Three out of 10 patients became seizure free after the epilepsy surgery or anti-epileptic drug treatment. Seizures in the 5 patients improved with the combination of anti-epileptic drugs. Two of 3 seizure free patients showed improved DQ (64%). Four of 7 uncontrolled seizure patients showed deteriorated DQ (57%). There is no statistical significance between seizure frequency and developmental outcome.

**Conclusions:** Frequent or continuous epileptic seizures may lead to elaboration of abnormal synaptic connections that are harmful to long-term development. It was found that children with EE underlying brain abnormalities that would inevitably lead to mental retardation in prognosis even their seizures stopped. The EE due to focal cortical lesions was shown excellent outcome after the surgery. Epilepsy surgery is an option for treating selected patients with EE due to unilateral, focal cortical lesions. This study supports the contention that early intervention affects developmental outcome.

### OP-10 ABERRANT IMMUNE ACTIVATION IN THE CENTRAL NERVOUS SYSTEM OF FEBRILE INFECTION-RELATED EPILEPSY SYNDROME (FIRES)

<u>Ayuko IGARASHI</u><sup>2)</sup>, Hiroshi SAKUMA<sup>1)</sup>, Tomonori SUZUKI<sup>1)</sup>, Kuniko KOHYAMA<sup>1)</sup>, Tomoko MIZUNO<sup>1)</sup>, Toshiaki SHIMIZU<sup>2)</sup>, Karin KOJIMA<sup>3)</sup>, Takanori YAMAGATA<sup>3)</sup>, Masaharu HAYASHI<sup>1)</sup>

- <sup>1)</sup> Department of Brain Development and Neural Regeneration, Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan
- <sup>2)</sup> Department of Pediatrics, Juntendo University Faculty of Medicine, Tokyo, Japan
- <sup>3)</sup> Department of Pediatrics, Jichi Medical University, Shimotsukeshi Tochigi, Japan

**Background:** Febrile infection-related epilepsy syndrome (FIRES) is a severe neurological disorder characterized by fever-induced repetitive and refractory partial seizures, which is followed by continuous transition to intractable epilepsy without a latent period. We previously reported that cerebrospinal fluid (CSF) levels of proinflammatory cytokines and chemokines were elevated in FIRES.

**Methods:** We assessed 28 children with FIRES, 31 children with other inflammatory neurological diseases (OIND) and 8 children with non-inflammatory neurological diseases patients(NIND) and report clinical and laboratory features, treatment, and outcome using a structured questionnaire and the levels of CSF biomarkers.

**Results:** CSF macrophage migration inhibitory factor (MIF) level was significantly higher in FIRES patients as compared to OIND and NIND. Other macrophage activation markers were also upregulated, although to a lesser extent, in FIRES.

**Discussion:** MIF is a proinflammatory cytokine that acts as an upstream mediator of innate immune response. It remains to be elucidated that how these immune activation drives refractory seizures and whether these biomarkers correlate with disease severity and outcome.

# ABSTRACTS

**Poster Presentation** 

#### P-01 RESTING-STATE NETWORKS IN AN INFANT WITH EARLY ONSET Epileptic ENCEPHALOPATHY WITH BURST-SUPPRESSION PATTERN ON EEG

<u>Hiroyuki KIDOKORO</u>, Yuji ITO, Chikako OGAWA, Atsuko OHNO, Yu OKAI, Tomohiko NAKATA, Yoko SAKAGUTI, Masahiro HAYAKAWA, Jun NATSUME Department of Pediatrics, Nagoya University Graduate School of Medicine, Nagoya, Japan

**Objective:** Burst-suppression (BS) pattern is an electroencephalography (EEG) pattern consisting of alternant periods of slow waves of high amplitude and periods of flat EEG. However, little is known about mechanism of BS. We presented here an infant with BS pattern on EEG who was diagnosed with congenital GPI anchor deficiency. The aim of this report was to identify the neural networks underlying BS pattern with resting-sate function MRI.

**Patient:** She was born at 37 weeks of gestation. Physiological examination revealed esophageal atresia, Hirshsprung disease and ichthyosis, later diagnosed with congenital glycophosphatidylinositol (GPI) anchor deficiency. 3T-conventional brain MRI revealed no structural abnormality but had white matter volume loss and myelination delay. EEG showed BS pattern from birth to 1 year of age or later. Vitamin B6 was administered from 3 months of age and was partially effective to reduce focal seizures.

**Resting-state fMRI:** Resting-state functional MRIs were performed twice, once at age 2 months and once at age 7 months. Analysis was done with independent component analysis. No existing RSNs commonly seen in term infants were identified at 2 months of age, but several functional networks, including sensory-motor, default mode, executive control were identified at 7 months of age, although EEG still showed BS pattern.

**Conclusion:** Even though BS pattern on EEG continues, RSNs may develop with time, indicating RSNs were organized independent of EEG activity.

### P-02

#### GOREISAN SUPPRESSES CEREBRAL EDEMA ASSOCIATED WITH HYPOXIC-ISCHEMIC ENCEPHALOPATHY IN CHILDHOOD RATS VIA THE INHIBITION OF AQUAPORIN 4

<u>Yoshiaki YANO<sup>1, 2)</sup></u>, Mitsumasa FUKUDA<sup>2)</sup>, Ryota MOTOIE<sup>2)</sup>, Shinji TSUDA<sup>2)</sup>, Kenta FUJIYAMA<sup>2)</sup>, Kouhei YOSHIMOTO<sup>2)</sup>, Yusuke IZUMO<sup>2)</sup>, Masanori ITO<sup>2)</sup>, Hajime YANO<sup>3)</sup>, Junya TANAKA<sup>3)</sup>, and Eiichi ISHII<sup>2)</sup>

- <sup>1)</sup> Department of Pediatrics, National Hospital Organization Ehime Medical Center, Toon, Ehime, Japan
- <sup>2)</sup> Department of Pediatrics, Ehime University Graduate School of Medicine, Toon, Ehime, Japan
- <sup>3)</sup> Department of Molecular and Cellular Physiology, Ehime University Graduate School of Medicine, Toon, Ehime, Japan

**Objectives:** Regulation of secondary cerebral edema is of prognostic significance in hypoxic-ischemic encephalopathy (HIE). Some studies have indicated that Goreisan, a traditional Japanese–Chinese herbal medicine, is effective in relieving adult brain edema. However, no study has reported its effectiveness in children or its pharmacological mechanism of action. Aquaporin 4 (AQP4) plays an important role in edematous formation. Therefore, we investigated the effects of Goreisan on HIE-associated brain edema and on AQP4 mRNA levels in childhood rats.

**Methods:** Twenty-six male Wister rats (21-day-old) were divided into Goreisan and control groups. We orally administered Goreisan (2 g/kg) and saline in Goreisan and control groups, respectively, 1 hr before surgery. After transient embolism (60 min) of the right middle cerebral artery using an embolic thread, the right common carotid artery was ligated and dissected. MRI (DWI and T2) was performed at 24 and 48 hr post-surgery, and survival rate was evaluated through day 14 post-surgery. Furthermore, 12 male Wister rats (21-day-old) were divided into the same two groups, and AQP4 mRNA was measured at 36 hr post-surgery.

**Results:** MRI results indicated that the affected area in the Goreisan group was significantly smaller than that in the control group at 24 (p = 0.004) and 48 hr (p = 0.007) post-surgery. The survival rate in the Goreisan group was significantly higher than that in the control group (p = 0.032). Finally, the Goreisan group showed significantly lower levels of AQP4 mRNA (p = 0.003).

**Conclusions:** Results from this study indicate that Goreisan suppresses brain edema associated with HIE, improving the survival rate. Moreover, it suppressed the expression of AQP4 mRNA in childhood rats. Future studies assessing specific ingredients of Goreisan, such as manganese and magnesium, are required to further examine its suppressive effect on the edema associated with childhood HIE.

#### P-03 POTENTIAL EFFECTS OF ANTIEPILEPTIC DRUGS ON GROWTH VELOCITY IN EPILEPTIC CHILDREN- EXPERIENCE IN ONE MEDICAL CENTER

Shyi-Jou CHEN<sup>1</sup>, Chien-Ming LIN<sup>1</sup>, Hueng-Chuen FAN<sup>2</sup>, and Der-Ming CHU<sup>1</sup>

<sup>1)</sup> Department of Pediatrics, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

<sup>2)</sup> Department of Pediatrics, Tungs' Taichung Metro Harbor Hospital, Taichung, Taiwan

**Objective:** The aim of this study was to investigate the potential effects of valproate (VPA) and/or oxcarbazepine (OXC) therapy on growth velocity and bone metabolism.

**Methods:** Seventy-three ambulatory children (40 boys and 33 girls) with epilepsy, aged between 1 and 18 years (mean age 9.8±4.1 years), were evaluated for growth velocity before and for one year after VPA and/or OXC treatment. The bone resorption marker serum tartrate-resistant acid phosphatase 5b (TRAcP5b) and the bone formation marker serum bone-specific alkaline phosphatase (BAP) were measured post-AEDs therapy for at least one year.

**Results:** The difference in growth velocity ( $\Delta$ Ht) and body weight change ( $\Delta$ Wt) between pre- and post-AEDs treatment were -1.0±2.8 cm/year (P < 0.05) and 0.1±3.9 kg/year (P = 0.84), respectively. The study population had serum TRAcP5b-SDS of -1.6±1.2 and BAP-SDS of 1.7±3.7 compared with sex- and age-matched healthy children. Significant correlation between serum TRAcP 5b and BAP activities was noted (r = 0.60, p < 0.001). There was a positive correlation between growth velocity and serum TRAcP 5b activity after AED treatment (r = 0.42, p < 0.01). No correlation was found between  $\Delta$ Ht,  $\Delta$ Wt, serum TRAcP 5b, BAP activity and types of AEDs.

**Conclusion:** Growth velocity was significantly decreased in epileptic children after one year of VPA and/or OXC treatment. The effect of VPA and/or OXC therapy on dysregulation of bone metabolism might have a potential role in physical growth. However, anextended prospective study should be approached to delineate this issue.

## TWO NOVEL SCN1A MUTATIONS IN TURKISH CHILDREN WITH DRAVET SYNDROME

P-04

Mutluay ARSLAN<sup>1</sup>, Sebahattin VURUCU<sup>1</sup>, Bülent ÜNAY<sup>1</sup>, Hande ÇAĞLAYAN<sup>2</sup>

<sup>1)</sup>Department of Pediatric Neurology, Gülhane Military Medical School, Ankara, Turkey

<sup>2)</sup>Department of Molecular Biology and Genetics, Boğaziçi University, İstanbul, Turkey

**Introduction:** Mutations in the gene encoding the  $\alpha 1$  subunit of the voltage gated sodium channel (*SCN1A*) are associated with Dravet syndrome. Despite over 1000 different SCN1A mutations reported, it is still hard to draw clear genotype-phenotype relationships.

**Case Presentation:** We report two patients with refractory seizures and psychomotor retardation in whom the final diagnosis was Dravet syndrome with confirmed mutations in the SCN1A gene. The first patient showed to have a c.4853-1 G>A(IVS25-1G>A, splice acceptor) transition in the SCN1A gene. The second patient had a heterozygous p.Thr1909 Ala (c.5725 A>G) mutation in exon 26.

**Conclusion:** Defining the clinical and genetic features of more cases with Dravet syndrome should provide new insights for the disease.

#### P-05 ACUTE ENCEPHALOPATHY ASSOCIATED WITH CHRONOLOGICAL EEG CHANGES AND A FATAL CLINICAL COURSE: A CASE STUDY

<u>Tetsuo KUBOTA</u><sup>1)</sup>, Takeshi SUZUKI<sup>1)</sup>, Tatsuya FUKASAWA<sup>1)</sup>, Tamiko Negoro<sup>1)</sup>, Yuma KITASE<sup>2)</sup>, Hiroyuki KIDOKORO<sup>2)</sup>, Jun NATSUME<sup>2)</sup>

<sup>1)</sup> Department of Pediatrics, Anjo Kosei Hospital, Anjo, Japan

<sup>2)</sup> Department of Pediatrics, Nagoya University, Nagoya, Japan

**Objective:** Acute infectious encephalitis/encephalopathy has several subtypes, which are differentiated according to magnetic resonance imaging (MRI) features. Acute encephalopathy with biphasic seizures and late reduced diffusion is a common subtype characterized by biphasic seizures and a "bright tree appearance" (BTA) on diffusion-weighted imaging (DWI). We report a case presenting with a high fever and status epilepticus. A subsequent DWI MRI showed BTA followed by fatal cerebral and brainstem edema.

**Case report:** A 4-year-old boy was referred to our hospital presenting with status epilepticus, a high fever, and coma (Glasgow coma scale; E1 V1 M2). Although no abnormal signs were apparent on the MRI, treatment with methylprednisolone pulse therapy (30 mg/kg/day for 3 days) and intravenous immunoglobulin (1 g/kg/day for 2 days) was initiated because of persistent disturbance of consciousness and abnormal changes in pupil size. We did not use therapeutic hypothermia to treat the patient. Chronological changes in the patient's clinical course were followed using serial encephalographic (EEG) recordings rather than continuous EEG monitoring. On day 2, the patient's EEG showed diffuse high-voltage slow waves with abnormal spindle-like activity (spindle coma). On day 3, we observed a decrease in slow waves and periods of discontinuous activity. The EEG showed low-voltage activity on day 4 and was flat on day 6. The MRI revealed cerebral edema and reduced diffusion in the subcortical white matter without central-sparing lesions on day 4 and fatal cerebral and brainstem edema on day 6. The patient died on day 13.

**Conclusion:** Continuous video-EEG monitoring is widely used in neonatal and adult intensive care units. EEG monitoring initiated immediately after hospital admission has considerable diagnostic value and may be useful for determining when to start treatment for acute encephalitis/encephalopathy.

## THE CHANGE OF ELECTROENCEPHALOGRAM CAN BE A POTENTIAL P-06

<u>Wang-Tso LEE<sup>1</sup></u>, Wen-Yu LU<sup>1</sup>, Jiann-Shing SHIEH<sup>2</sup>

<sup>1)</sup> Department of Pediatrics, National Taiwan University Hospital, Taipei, Taiwan

<sup>2)</sup> Department of Mechanical Engineering, Yuan Ze University, Taoyuan, Taiwan

**Objective:** Various analytic measures had been used to investigate the change of brain complexity with age. This study wanted to investigate the relationship between later epilepsy and the changes of electroencephalogram (EEG) complexity in neonatal seizures.

**Methods:** EEG signals from 32 neonates below 2 months old were enrolled. The neonates were classified into 3 groups: 9 were normal controls, 9 were neonatal seizures without later epilepsy, and 14 were neonatal seizures with later epilepsy. Sample entropy (SamEn), multiscale entropy (MSE) and complexity index (CI) were analyzed.

**Results:** There were no significant changes in SamEn, but the CI values showed significantly decreased in Channels C3, C4, and Cz for infants with neonatal seizures and later epilepsy compared with control group. More multifocal epileptiform discharges in EEG, more abnormal neuroimaging findings, and higher incidence of future developmental delay were noted in the group with later epilepsy.

**Conclusions:** Decreased MSE and CI values may arise from the mixed effects of acute insults, underlying brain immaturity, and prolonged seizures-related damage. MSE and CI can provide a quantifiable and potential predictor to the outcome of neonatal seizures.

### P-07 SERUM N-TERMINAL PRO-B-TYPE NATRIURETIC PEPTIDE LEVELS ARE ELEVATED DURING ACUTE ENCEPHALOPATHY

<u>Miho FUKUI</u><sup>1)</sup>, Shuichi SHIMAKAWA<sup>1)</sup>, Takuya MATSUDA<sup>1)</sup>, Mari HATANAKA<sup>1)</sup>, Atsushi MORI<sup>1)</sup>, Hiromitsu TOSHIKAWA<sup>1)</sup>, Chizu OHBA<sup>2)</sup>, Mitsuru KASHIWAGI<sup>2)</sup>, Ryohei MIYAMOTO<sup>3)</sup>, Shohei NOMURA<sup>4)</sup>, Kohji AZUMAGAWA<sup>4)</sup>, Takuya TANABE<sup>5)</sup>, Hiroshi TAMAI<sup>1)</sup>

- <sup>1)</sup>Department of Pediatrics, Osaka Medical College, Osaka, Japan
- <sup>2)</sup> Department of Pediatrics, Hirakata Municipal Hospital, Osaka, Japan
- <sup>3)</sup>Department of Pediatrics, Miyamoto Children's Clinic, Osaka, Japan
- <sup>4)</sup>Department of Pediatrics, Seikeikai Hospital, Osaka, Japan
- <sup>5)</sup> Department of Pediatric Neurology, Tanabe Children's Clinic, Osaka, Japan

Acute virus-associated encephalopathy induces seizures. Serum N-terminal pro-Btype natriuretic peptide (NTproBNP) levels are elevated following febrile and afebrile seizures. However, the role of NTproBNP in acute virus-associated encephalopathy pathology is unknown. The present study assessed whether increased serum secretion of NTproBNP during the acute phase of acute virus-associated encephalopathy associated with convulsion. We enrolled 11 patients with acute virus-associated encephalopathy and convulsions (E group: 7 boys, 4 girls; median age, 3.00±1.92 years) and 130 patients with febrile seizure (FS group: 80 boys, 50 girls; median age, 3.23±2.44 years). The E group had significantly higher NTproBNP levels (420±283 pg/ml) compared with FS group  $(166\pm 228 \text{ pg/ml})$  (P< 0.0005). Furthermore, subjects with prolonged seizure within the E group had significantly higher NTproBNP levels (428±343 pg/ml) compared with subjects with prolonged seizure within the FS group  $(134\pm100 \text{ pg/ml})$  (P<0.005). Furthermore, because previous reports show that NTproBNP levels are 80±93 pg/ml in healthy infants and 64±43 pg/ml in healthy children, serum NTproBNP levels might be elevated in cases of acute virus-associated encephalopathy associated with convulsion compared with healthy controls. Our findings suggest that serum NTproBNP levels are increased during the acute phase of acute virus-associated encephalopathy associated with convulsion. NTproBNP might be useful biomarker for acute virus-associated encephalopathy associated with convulsions in children.

#### SEIZURE CHARACTERISTICS OF EPILEPSY IN CHILDHOOD AFTER ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION

<u>Yuji ITO</u>, Jun NATSUME, Hiroyuki KIDOKORO, Yu OKAI, Chikako OGAWA, Atsuko ONO, Tomohiko NAKATA, Tamiko NEGORO and Kazuyoshi WATANABE Department of Pediatrics, Nagoya University Graduate School of Medicine, Aichi, Japan

**Objective:** The aim of this study was to clarify characteristics of post-encephalopathic epilepsy (PEE) in children after acute encephalopathy with biphasic seizures and late reduced diffusion (AESD), paying particular attention to precise diagnosis of seizure types.

**Methods:** Among 262 children with acute encephalopathy/encephalitis registered in a database of the Tokai Pediatric Neurology Society between 2005 and 2012, 44 were diagnosed with AESD from the clinical course and MRI findings and were included in this study. Medical records were reviewed to investigate clinical data, MRI findings, neurological outcomes, and presence or absence of PEE. Seizure types of PEE were determined by both clinical observation by pediatric neurologists and ictal video-electroencephalogram recordings.

**Results:** Of the 44 patients after AESD, 10 (23%) had PEE. The period between the onset of encephalopathy and PEE ranged from 2 to 39 months (median: 8.5 months). Cognitive impairment was more severe in patients with PEE than in those without. Biphasic seizures and status epilepticus during the acute phase of encephalopathy did not influence the risk of PEE. The most common seizure type of PEE on clinical observation was focal seizures (n = 5), followed by epileptic spasms (n = 4), myoclonic seizures (n = 3), and tonic seizures (n = 2). In 6 patients with PEE, seizures were induced by sudden unexpected sounds. Seizure types confirmed by ictal video-electroencephalography recordings were epileptic spasms and focal seizures with frontal onset, and all focal seizures were startle seizures induced by sudden acoustic stimulation. Intractable daily seizures remain in 6 patients with PEE.

**Significance:** We demonstrate seizure characteristics of PEE in children after AESD. Epileptic spasms and startle focal seizures are common seizure types. The specific seizure types may be determined by the pattern of diffuse subcortical white matter injury in AESD and age-dependent reorganization of the brain network.

#### P-09 DISRUPTED GLUTAMATE-GLUTAMINE CYCLE IN ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION(AESD)

<u>Eri OGUNI</u><sup>1)</sup>, Jun-ichi TAKANASHI<sup>1)</sup>, Takafumi HONDA<sup>1)</sup>, Kumi YASUKAWA<sup>1)</sup>, Masashi MIZUGUCHI<sup>2)</sup>

- <sup>1)</sup> Department of Pediatrics, Tokyo Women's Medical University Yachiyo Medical Center, Yachiyo, Japan
- <sup>2)</sup> Department of Developmental Medical Sciences, Graduate School of Medicine, the University of Tokyo, Tokyo, Japan

**Objective:** Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is the most common subtype of infectious pediatric encephalopathy in Japan. It is sometimes difficult to make an early diagnosis of AESD; excitotoxicity is postulated to be the pathogenesis based on elevated glutamine (Gln) and glutamate (Glu) complex (Glx=Glu+Gln) observed on MR spectroscopy. It is uncertain whether Gln or Glu contributes to the elevated Glx, or whether MR spectroscopy is useful for an early diagnosis.

**Methods:** Seven Japanese patients with AESD (five boys and two girls, 11 month to 1 year of age) were enrolled in this study. MR spectroscopy was acquired from the frontal white matter(TR of 5000 msec, TE of 30 msec)with a 1.5 or 3.0 tesla scanner. MR spectroscopy was performed 4 times for two patients, 3 times for 1 patient, twice for 3 patients, and once for 1 patient. Quantification of Glu and Gln was performed using LCModel.

**Results:** Glu was elevated in 4 of 5 studies on days 1-4 before the bright tree appearance on DWI, and became normal or low afterwards. Gln was normal in 3 studies on days 1-2, elevated in all 9 studies on days 4-12, and became normal or low afterwards.

**Conclusion**: These findings suggest that elevated Glx observed on MR spectroscopy may be useful for an early diagnosis. Acute Glu elevation changes to subacute Gln elevation, suggesting a disrupted Glu-Glncycle may play an important role.

## PAROXYSMAL SYMPATHETIC HYPERACTIVITY DURING THERAPEUTIC HYPOTHERIMIA IN A CASE WITH SEVERE AESD

**P-10** 

<u>Yuko ICHIMIYA<sup>1), 2)</sup></u>, Yasunari SAKAI<sup>1)</sup>, Noriyuki KAKU<sup>1), 2)</sup>, Fumiya YAMASHITA<sup>1)</sup>, Wakato MATSUOKA<sup>1), 2)</sup>, Soichi MIZUGUCHI<sup>1), 2)</sup>, Yuichiro HIRATA<sup>1), 2)</sup>, Yoshito ISHIZAKI<sup>1)</sup>, Masafumi SANEFUJI<sup>1)</sup>, Hiroyuki TORISU<sup>1), 3)</sup>, Hidetoshi TAKADA<sup>1)</sup>, Yoshihiko MAEHARA<sup>2)</sup>

<sup>1)</sup>Department of Pediatrics, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

<sup>2)</sup> Emergency and Critical Care Center, Kyushu University, Fukuoka, Japan

<sup>3)</sup>Department of Pediatrics, Fukuoka Dental College Medical and Dental Hospital, Fukuoka, Japan

**Introduction:** Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is the most common form of pediatric acute encephalopathy in Japan. Little is known about the relationships between the neuroimaging features and complications during the acute phase of AESD. We herein report a case with severe AESD, who developed transient paroxysmal sympathetic hyperactivity (PSH), an episodic syndrome which usually occurs after various brain injury, commonly after brain trauma.

Case presentation: The patient was a 3-year-old male. He was born to healthy, nonconsanguineous parents at 41 weeks with 3,012 g of birth weight. Severe (Apgar score 2 at 5 min) but transient asphyxia was noted at birth. The developmental quotient was evaluated to be 45 at 18 months of age. He experienced the first attack of seizure at 2 years and 4 months of age, and began to take valproic acid thereafter. He was brought to the emergency department of our hospital for right hemi-convulsions with a precedent episode of viral infection. The seizure was terminated by infusions of diazepam and midazolam, whereas his consciousness did not recover during the first 3 days. Serial brain MRI scans started to show the bright-tree appearance at the left parieto-occipital region on the 3rd day, which extended to the whole subcortical regions by the 7th day. With an immediate diagnosis of AESD, therapeutic hypothermia at 34°C was conducted. On the 6th day, intermittent mydriasis accompanying increased heart rates and blood pressure was noted during the hypothermia, which occurred several times a day. Since the followup studies excluded the possibilities of elevated intracranial pressure, infection, convulsion and withdrawal syndrome, he was finally diagnosed as having PSH as the cause of these symptoms.

**Conclusion:** This is the first report demonstrating that PSH should be considered as one of neurological complications in the acute phase of severe AESD.

#### P-11 INTRAVENOUS IMMUNOGLOBULIN TREATMENT FOR PATIENTS WITH POSTENCEPHALOPATHIC EPILEPSY AFTER ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION

<u>Kenji INOUE</u>, Tomohiro KUMADA, Minoru SHIBATA, Ikuko HIEJIMA, Akihito NOZAKI, Anri HAYASHI, Mioko MORI, Saeko SASAKI, Tatsuya FUJII, Taro YAMADA, Kenji FUJI, and Takashi UENO Department of Pediatrics, Shiga Medical Center for Children, Shiga, Japan

**Introduction:** Postencephalopathic epilepsy (PEE) is a well-recognized, serious complication of acute encephalopathy, and is characterized by intractable seizures. Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is the most common acute infection-associated encephalopathy syndrome in childhood and is associated with a high incidence of neurologic sequelae, including PEE. Although the pathogenesis of PEE remains unclear, autoimmune mechanisms have been speculated

recently. Immunotherapy, such as steroid or intravenous immunoglobulin (IVIG) therapy, has been reported to be effective in some patients with PEE. We report 2 children with PEE after AESD treated with IVIG.

**Patients:** Patient 1 developed AESD at the age of 1 year 4 months. Four months thereafter, epileptic spasms with clustering occurred about 10 times per day. Serum test for glutamic acid decarboxylase (GAD) antibody was negative. The seizures were intractable with multiple antiepileptic drugs. At the age of 2 years, IVIG treatment was started monthly. After the first administration of IVIG, seizures ceased, although they recurred 3 months after the IVIG treatment.

Patient 2 developed AESD at the age of 1 year 10 months. Six months thereafter, epileptic spasms with clustering occurred about 10 times per day. Serum test for GAD antibody was positive. The seizures were intractable with multiple antiepileptic drugs. At the age of 4 years, IVIG treatment was started monthly. 5 months after the start of the IVIG treatment, seizures ceased. The patient has now been seizure-free for 4 months since.

**Discussion:** Immunotherapy has been reported to be more effective in patients with autoimmune epilepsy with antibodies such as GAD antibody than in those without. Patient 2 with GAD antibody showed a better response to IVIG treatment than patient 1 without it. IVIG may be considered for the treatment of PEE after AESD, especially in patients with autoimmune antibodies.

#### DISTINGUISHING ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUSED DIFFUSION FROM PROLONGED FEBRILE SEIZURES BY ACUTE PHASE EEG SPECTRUM ANALYSIS

Masayoshi OGURI<sup>1</sup>, Yoshiaki SAITO<sup>1</sup>, Chisako FUKUDA<sup>2</sup>, and Yoshihiro MAEGAKI<sup>1</sup>

- <sup>1)</sup> Division of Child Neurology, Department of Brain and Neurosciences, Faculty of Medicine, Tottori University, Yonago, Japan
- <sup>2)</sup> Department of Pathobiological Science and Technology, School of Life Sciences, Faculty of Medicine, Tottori University, Yonago, Japan

**Objective:** To differentiate the features of electroencephalography (EEG) after status epileptics in febrile children with final diagnosis of either acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) or febrile seizure (FS) for an early diagnosis.

**Methods:** We retrospectively collected data from 37 children who had status epilepticus and for whom EEGs were recorded within 120 hours. These included subjects with a final diagnosis of acute encephalopathy with biphasic seizures and late reduced diffusion (n = 17) and febrile seizures (n = 20). Initially, all EEGs were visually assessed and graded, and correlation with outcome was explored. Representative EEG epochs were then selected for quantitative analyses. Furthermore, data from AESD (n = 7) and FS (n = 16) patients for whom EEG was recorded within 24 hours were also compared.

**Results:** The outcome of the moderate EEG severity group was variable and was not predictable from visual inspection. Frequency band analysis revealed that although solid delta power was not significantly different between AESD and FS, the AESD group showed lower power than the FS group at the frontal area in the alpha, beta, and gamma band. The band powers showed earlier improvement towards 24 hour in FS than in AESD.

**Conclusion:** Sequential EEG recording up to 24 hours from onset appeared to be helpful for distinction of AESD from FS before emergence of the second phase of AESD.

#### P-13 SEQUENTIAL GLASGOW COMA SCALE EVALUATION IS THE MOST WORTHWHILE WAY FOR EARLY DETECTION OF ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION

<u>Tetsuhiro FUKUYAMA</u><sup>1)</sup>, Shunsuke AMAGASA<sup>2)</sup>, Taku SASAKI<sup>1)</sup>, Hideko NAKAJIMA<sup>1)</sup>, Hikoro MATSUI<sup>2)</sup>, Noboru FUEKI<sup>3)</sup>, and Shinichi HIRABAYASHI<sup>1)</sup>

<sup>1)</sup> Division of Neurology, Nagano Children's Hospital, Azumino, Japan

<sup>2)</sup> Department of Pediatric Intensive Care, Nagano Children's Hospital, Azumino, Japan

<sup>3)</sup> Department of Rehabilitation, Nagano Children's Hospital, Azumino, Japan

**Objective:** Recently, some scoring systems for differentiating patients with acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) from patients with prolonged febrile seizure (PFS) were proposed. But some AESD cases don't start as status epilepticus. Therefore, we evaluated Glasgow Coma Scale (GCS) and laboratory data in acute phase on our patients to distinguish AESD and complex febrile seizure (CFS). We also evaluated two scoring systems which were proposed by Tada etal.and Yokochi et al. in our patients.

**Methods:** We retrospectively reviewed medical records of patients younger than 6 years old admitted to Nagano Children's hospital with CFS from April 2009 to March 2015. We classified the participants into CFS group and AESD group. We evaluated sequential GCS and Laboratory data within 24 hours after first seizure among both groups.

**Results:** 9 AESD patients and 101 CFS patients were enrolled in this study. In the evaluation of consciousness, GCS at 12 and 24 hours after onset was significantly lower in AESD group than CFS ( $p \le 0.05$ ). Furthermore, while GCS improves over time in CFS group, recovery of AESD group was insufficient from 6 hours after onset. Almost laboratory data were not significantly different between two groups. GCS  $\le 14$  at 12 hours after onset and no improvement in GCS  $\ge 2$  from 6 to 12 hours had a sensitivity of 86% and specificity of 95% for the diagnosis of AESD. Sensitivity and specificity of Tada's scoring system for the diagnosis of AESD in our patients were 67% and 91%. Those of Yokochi's scoring system were 44% and 94%. In particular, AESD patients without PFS missed correct diagnosis by both scoring systems.

**Conclusion:** Sequential GCS evaluation is the most worthwhile way for the early detection of AESD.

#### DEXTROMETHORPHAN AND CYCLOSPORINE A FOR ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION

<u>Toshiyuki MAEDA</u><sup>1)</sup>, Keiko HIRABARU<sup>1)</sup>, Nobuyasu ONO<sup>2)</sup>, Daisuke TAJIMA<sup>2)</sup>, Muneaki MATSUO<sup>1)</sup>

<sup>1)</sup>Department of Pediatrics, Faculty of Medicine, Saga University, Saga, Japan

<sup>2)</sup>Department of Pediatrics, Ureshino Medical Center, Saga, Japan

**Objectives:** Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is a recently established encephalopathy syndrome. The outcome of AESD is characterized by low mortality rate and high incidence of neurologic sequelae. Although the exact pathogenesis remains uncertain, excitotoxic injury with delayed neuronal death is proposed. On the basis of this hypothesis, we tried a combination therapy of N-methyl-D-aspartate receptor antagonist, dextromethorphan, and apoptosis inhibitor, cyclosporine A, in seven patients with AESD.

**Patients and methods:** Seven patients with AESD (4 females and 3 males, median age 1.5 years, range 0.6-8 years) were retrospectively analyzed. The duration of the early seizure ranged from 30 to 150 min (median, 60 min). All patients had a biphasic clinical course. Late seizure appeared from 3 to 5 days of illness (median, 3.0 days). The therapeutic protocol was as follows: (1) Patients showing mild (<30 on the Japan Coma Scale) consciousness disturbance 24 hours after prolonged(>15 minutes) febrile seizures were started on oral dextromethorphan 2mg/kg/d for 5 days. (2) After the diagnosis of AESD, continuous intravenous infusion of cyclosporine A (2 mg/kg/d) was administered for 7 days.

**Results:** Dextromethorphan was started on the second day after first seizure in two patients, and the other five patients was started it on the day of late seizure. The abnormal lesions on the magnetic resonance imaging were disappeared soon, but single photon emission tomography after several months showed decreased focal cerebral blood flow. All patients recovered without severe neurologic sequelae, except for hyperactivity in two patients and mild hemiparesis in one patient. Two patients who was administered dextromethorphan before late seizures, were almost completely recovered without neurological sequelae.

**Conclusions:** The combination regimen of dextromethorphan and cyclosporine A could be effective for the treatment of AESD. Furthermore, the earlier administration of dextromethorphan might be the more effective.

#### A CASE OF DRAVET SYNDROME AFFECTED AN ACUTE ENCEPHALOPATHY

<u>Tatsuyuki SOKODA</u><sup>1)</sup>, Yuka NISHIZAWA<sup>1)</sup>, Jun MATSUI<sup>1)</sup>, Noriko NISHIKURA<sup>1)</sup>, Tomoyuki TAKANO<sup>1)</sup>, Yoshihiro TAKEUCHI<sup>1)</sup>, Atsushi ISHII<sup>2)</sup>, Shinichi HIROSE<sup>2)</sup>

<sup>1)</sup> Department of Pediatrics, Shiga University of Medical Science, Shiga, Japan

**P-15** 

<sup>2)</sup> Department of Pediatrics, School of Medicine, Fukuoka University, Fukuoka, Japan

**Introduction:** Although patients with Dravet syndrome (DS) are known to be predisposed to acute encephalopathy, no etiology for progressing to such encephalopathy has been established.

**Case:** The patient was a 6-year-old Japanese girl who began to present with seizures at the age of 3 months. She was diagnosed as DS at the age of 1 year by SCNIA gene test. Following diagnosis, various antiepileptic drugs were administrated to control her intractable seizures. At the age of 6 years and 9 months, she experienced a prolonged seizure, leading to urgent hospitalization. Routine blood examination, brain CT scan, and lumbar puncture were performed in emergency, without previous diagnostic data. During this period, the girl presented with disturbed consciousness, and her condition was classified as Glasgow Coma Scale score of 7. At this time, her EEG showed slow diffuse waves of mainly theta band waves, which indicated some improvement on the following day; however, her consciousness remained unaltered. On the seventh day of hospitalization, her brain MRI scan presented a remarkably reduced diffusion in the bilateral subcortical white matter of the frontal lobe, but no seizure was observed since the hospitalization. Prior to the seizure, the girl could walk without support and speak several words. However, following discharge, she developed severe neurological and motor sequela, such as wheelchair-mobile, lack of coherent speech, and frequent involuntary movements.

**Discussion:** There are few reports about acute encephalopathy in children with DS whereas most patients of those shows poor neurological outcomes that were similar to our patient. Brain MRI of our patient presented late reduced diffusion pattern ("bright tree appearance"), which is typical of acute encephalopathy with biphasic-seizures; however, seizure recurrence was not observed. Hence, it is not clear if the poor outcome and neuroimaging characteristics are specific for acute encephalopathy with DS or are incidental.

#### CASE SERIES OF FATAL ACUTE ENCEPHALOPATHY

<u>Kazumi TOMIOKA</u><sup>1)</sup>, Hiroaki NAGASE<sup>1), 2)</sup>, Yusuke ISHIDA<sup>2)</sup>, Tsukasa TANAKA<sup>2)</sup>, Masahiro NISHIYAMA<sup>1), 2)</sup>, Kyoko FUJITA<sup>2)</sup>, Daisaku TOYOSHIMA<sup>2)</sup>, Azusa MARUYAMA<sup>2)</sup>, Masaaki MATSUMOTO<sup>1)</sup>, Ai UNZAKI<sup>1)</sup>, Hiroyuki AWANO<sup>1)</sup>, Hiroki TAKEDA<sup>3)</sup>, Yoshiyuki UETANI<sup>3)</sup>, Satoshi TAKADA<sup>4)</sup>, and Kazumoto IIJIMA<sup>1)</sup>

<sup>1)</sup> Department of Pediatrics, Kobe University Graduate School of Medicine, Kobe, Japan,

<sup>2)</sup> Department of Neurology, Hyogo Prefectural Kobe Children's Hospital, Kobe, Japan,

- <sup>3)</sup> Department of Emergency and Critical Care Medicine, Hyogo Prefectural Kobe Children's Hospital, Kobe, Japan,
- <sup>4)</sup>Kobe University Graduate School of Health Science, Kobe, Japan

**Objective:** The detailed clinical course of fatal acute encephalopathy has yet to be widely published. The objective of this study was to describe the detailed clinical course of fatal acute encephalopathy.

**Methods:** We retrospectively reviewed the medical records of 5 patients (6 months to 14 years) who: 1) previously had no neurological disorders, 2) diagnosed as acute encephalopathy, and 3) left hospital mortality between October 2002 and March 2015 at Hyogo Prefectural Kobe Children's Hospital.

**Results:** The median body temperature on admission was 39.6°C. The initial neurological symptom was convulsion (3 patients) or impaired consciousness (2 patients). An abnormality on the initial head CT was detected in only 1 patient. All patients met SIRS criteria at 1-11 hours after onset defined as appearance of initial neurological symptom, 4 patients developed shock at 4-13 hours after onset, 4 patients met DIC criteria at 4-11 hours after onset. Steroid pulse therapy was administered in 3 patients at 3-9 hours after onset, and targeted temperature management was administered in 1 patient at 8 hours after onset. Subjects could be classified as syndromes of acute encephalopathy at 1-11 hours after onset. Two, one, and 5 patients were classified as HSES, ANE and Reye-like syndrome, respectively (with some patients being categorized as having more than one syndromes). The state of brain death was declared from 8 hours to 4 days after onset.

**Conclusion:** Most cases of fatal acute encephalopathy developed shock and DIC within several hours after initial neurological symptom. The initial head CT rarely leads the definite diagnosis of acute encephalopathy. Steroid pulse therapy administered within 3-9 hours after onset was ineffective. Earlier diagnosis and intervention within the first few hours after onset is indicated to decrease the number of fatal acute encephalopathy.

#### P-17 A CASE REPORT WITH LATE-ONSET MAPLE SYRUP URINE DISEASE PRESENTED AS EPILEPTIC ENCEPHALOPATHY

#### Meltem UZUN, and Cengiz HAVALI

Dortcelik Children Hospital, Turkey

Epileptic encephalopathies are severe brain disorders of early age that manifest with seizures, cognitive, behavioural, and neurological deficits. Epileptic encephalopathy can be induced by inborn metabolic defects. Amino acidopathies present with seizures and cognitive, behavioural, or motor disturbances resulting from the accumulation of toxic intermediaries, or possible structural damage. Some may induce an epileptic encephalopathy.

Maple syrup urine disease is a disorder of branched-chain keto acid metabolism. Five distinct clinical variants can be distinguished, based on the age of onset, severity of clinical symptoms and response to thiamine treatment; classical and non-classical forms. Classic maple syrup urine disease is the most common form, with symptoms developing in neonates aged 4-7 days. In cases of non-classic maple syrup urine disease, onset may be later and symptoms may vary.

A six-month-old boy was diagnosed with maple syrup urine disease admitted hospital with epileptic encephalopathy. Clinical features were characterized by lethargy, seizures, and motor retardation. High-performance liquid chromatography of the urine and serum revealed elevated levels of branched-chain amino acids. Magnetic resonance imaging showed diffuse hyperintense signals in the white matter along deep cerebellar white matter, dorsal part of the brainstem, the cerebral peduncles, and the dorsal limb of the internal capsule, thalami, and globus pallidus. There was burst-suppression pattern on his electroencephalography.

Maple syrup urine disease is a treatable disease. Although, encephalopathy is common in classical form seen during newborn period it can be seen in non-classical forms during late period. Therefore, maple syrup urine disease should be suspected in cases of epileptic encephalopathy.

#### A CASE OF SEVERE HYPOGLYCEMIC ENCEPHALOPATHY CAUSED BY HYPOCARNITINEMIA DUE TO CEFTERAM PIVOXIL

**P-18** 

<u>Kaori SASSA</u>, Yuichi ABE, Yuki MINAMIKAWA-SHIMIZU, Eiji MORITA, Akira OHTAKE, Hideo YAMANOUCHI Department of Pediatrics, Saitama Medical University, Japan

**Objective:** We report here a case of severe hypoglycemic encephalopathy caused by hypocarnitinemia due to cefteram pivoxil,

**Case report:** This one-year old boy was referred to our hospital for prolonged comatose state after convulsions associated with fever. He was a product of 30 weeks' gestation delivered by caesarian section, weighing 593 g at birth. His Apgar scores were 7 at 1 min. He was diagnosed as extremely low birth weight infant caused by intrauterine growth retardation. His developmental millstones were normal; walking alone at 13 months and speaking several words at 10 months of his corrected age. At one year, he developed prolonged comatose state, following three times of generalized convulsions associated with fever after six-day administration of cefteram pivoxil. On admission, his height was 73.8cm (-2.9SD) and weight was 7.2kg (-3.4SD). Neurological examinations showed sluggish light reflexes as well as mild spasticity in the left upper limb and bilaterally positive Babinski reflexes. Laboratory studies showed hypoglycemia (26mg/dl) and hyperammonemia (NH3 440 µg/dl). Diffusion-weighted MR image showed high signal in subcortical white matter of bilateral frontal lobes. 99<sup>m</sup>Tc-ECD SPECT exhibited decreased cerebral blood flow in the bilateral frontal lobes. Tandem mass screening tests showed decrease in serum free carnitine as 8.5nmol/ml, and increase in C5 carnitine (derived form pivaloylcarnitine) as 3.30nmol/ml, leading the diagnosis of acute encephalopathy associated with secondary hypocarnitinemia due to cefteram pivoxil. He was treated with mild hypothermia therapy combined with intravenous administration of high dose of methylprednisolone 30mg/kg/day and L-carnitine 80mg/kg/day. He is now 3 years and has become confined to his bed for severe neurological sequelae with paralysis of the extremities.

**Conclusion:** From our experience, it should be noted that the possibility of acute encephalopathy due to hypocarnitinemia is considered in a case of administration of cefteram pivoxil, pivalic acid-containing antibiotic.

### P-19 SIBLINGS WITH LIMBIC ENCEPHALITIS

<u>Sho NARAHARA</u>, Yusuke AOKI, Motomasa SUZUKI, Kazuya ITOMI Department of Pediatric Neurology, Aichi Children's Health and Medical Center, Obu, Japan

**Introduction:** Familial cases of limbic encephalitis are rare. We report siblings with limbic encephalitis.

**Case 1:** A four-year-old girl presented with status epilepticus, following involuntary movements of her legs and nocturnal enuresis about a month before. She developed hypoactivity, orofacial dyskinesia, excessive sweating, and stereotypical behavior. Three weeks after the onset, her consciousness fluctuated between agitation and stupor. Her previous doctor diagnosed limbic encephalitis, and began corticosteroid pulse therapy and intravenous immunoglobulin therapy. Thirty days after the onset, she was transferred to our hospital. Brain MRI and SPECT were normal. Electroencephalogram showed diffuse high-voltage slow waves. No anti-neuronal antibodies including anti-NMDAR antibodies were detected. Our examination found no tumor. Fifty one days after the onset, we applied plasmapheresis and then her consciousness and verbal functions began to recover. She was discharged with almost the same of her premorbid functioning 138 days after the onset.

**Case 2:** A nine-year-old boy presented with involuntary movements of his legs. He is the brother of the above patient. He developed dysthymia, decreased responsiveness, low grade fever, and excessive sweating. Twenty days after the onset, he was admitted to our hospital for clusters of seizures. Brain MRI and SPECT was normal. Electroencephalogram showed frontal high-voltage slow waves. Anti NMDAR antibodies were not detected. Our examination found no tumor. We diagnosed limbic encephalitis and began corticosteroid pulse therapy. However, his mood and responsiveness did not improve. Furthermore, he developed agitation and abnormal behavior. We applied plasmapheresis, and then his responsiveness improved. Because dysthymia still remained, we carried out corticosteroid pulse therapy again and intravenous immunoglobulin therapy. He got able to keep his temper and was discharged 52 days after the onset.

**Discussion:** Siblings with limbic encephalitis may suggest the presence of genetic factors.

#### ACUTE DISSEMINATED ENCEPHALOMYELITIS: CLINICAL PROFILE, MAGNETIC RESONANCE IMAGING FINDINGS AND OUTCOME IN A COHORT OF 35 CHILDREN

<u>Bindu Parayil SANKARAN</u><sup>1)</sup>, Divya Raj R<sup>1)</sup>, Rose Dawn BHARATH<sup>2)</sup>, Anita MAHADEVAN<sup>3)</sup>, Vani SANTHOSH<sup>3)</sup>

<sup>1)</sup> Depts of Neurology, National Institute of Mental Health And Neurosciences, Bangalore, India

- <sup>2)</sup> Depts of Neuroimaging and interventional Radiology, National Institute of Mental Health &Neurosciences, Bangalore, India
- <sup>3)</sup> Department of Neuropathology, National Institute of Mental Health & Neurosciences, Bangalore, India.

**Objectives:** To evaluate the clinical profile, magnetic resonance imaging findings and outcome in a cohort of children with acute disseminated encephalomyelitis (ADEM) classified based on the international pediatric multiple sclerosis criteria (IPMS), 2007.

**Methods:** The study included 35 children [Mean age 8.2 years, Range 3-17yrs, M: F, 1.2:1] with a diagnosis of ADEM seen over a period of 10 years (2003- 2013). All satisfied the consensus definitions by IPMS. Clinical profile, magnetic resonance imaging findings and outcome in these patients were analyzed

**Results:** A prodromal illness was noted in 31 (88.5%) patients, majority being upper respiratory tract infections. The clinical findings included encephalopathy (100%), pyramidal signs (37%), cerebellar signs (25%), cranial nerve palsies (22%), seizures (22%), myelopathy (17%), brain stem signs(17%) & optic neuritis (14%). CSF study available in 28 patients showed pleocytosis in 9, increased protein in 9 and oligo clonal bands in 4. Magnetic resonance imaging showed lesions in juxta cortical region (68%), lobar white matter (51%), periventricular white matter (31%), thalamus (23%), basal ganglia (17%), middle cerebellar peduncle (14%), brainstem (40%) and cerebellar white matter (25%). Other features included contrast enhancement (13/27), & diffusion restriction (8/26). All patients except two received intravenous methyl prednisolone in doses of 20-30 mg/ kg for five days followed by oral steroids. Follow up data in 31 patients (mean period of follow up 18  $\pm$  21 months, range 1mo - 9yrs) showed that, all but two patients had a good functional outcome on modified Rankin scale. One patient had fulminant form of ADEM and expired during the acute illness. None had recurrent or multiphasic ADEM.

**Conclusion:** The present series demonstrates that ADEM in children has a polysymptomatic presentation and good outcome. It also highlights that IPMS criteria help in correct classification & prognostication in children with acute demyelinating disorders.

#### P-21 A COMPARATIVE STUDY OF TWO CHILD CASES OF ANTI-NMDA RECEPTOR ENCEPHALITIS IN OUR HOSPITAL

<u>Sotaro YUZAWA</u>, Daiki TAKI, Fumiko IWAI, Hiroaki MURAKAMI, Yuki MATSUHISA, Hideki MATSUMOTO, Emiko KOBAYASHI, Kunihiro MATSUNAMI, Eiji MATSUKUMA, Atsushi IMAMURA

Department of pediatrics, Gifu prefectual general medical center, Japan

**Objective:** Anti-N-methyl-D-aspartate (NMDA) receptor encephalitis is classified as an autoimmune type of encephalitis, which was proposed as paraneoplastic encephalitis associated with NMDA receptor, one of glutamate receptor. This disease frequently occurs in young women with ovarian teratoma, regardless of sex, age and the existence of tumors.

**Methods:** We compared the clinical features and course of two cases of Anti-NMDA receptor encephalitis in our hospital.

**Results:** The patients were 2-year-old girl and 5-year-old boy, having anti-NMDA receptor antibodies in their cerebrospinal fluid. They revealed typical clinical features of NMDA receptor encephalitis, and their hospitalizations were also about 60 days. Head MRI was performed but it revealed no remarkable findings in them. There was no tumors including ovarian teratoma in them. Tracheal intubation was not performed, but tube feeding was needed in them. Methylprednisolone and intravenous immunoglobulin (IVIG) were administered to them. Antiepileptic drugs were administered to the boy, but not to the girl.

**Conclusion:** We have experienced two cases of anti-NMDA receptor encephalitis. Their clinical symptoms were gradually improved, however the therapy of steroid and IVIG did not seems to be effective. We report here the rare cases of anti-NMDA receptor encephalitis with younger onset and no tumors.

#### DIFFERENCE OF RESPONSE TO KETOGENIC DIET IN 2 CHILDREN WITH ACUTE ENCEPHALITIS WITH REFRACTORY, REPETITIVE PARTIAL SEIZURES

<u>Yu OKAI</u>, Atsuko ONO, Hiroyuki KIDOKORO, Yoko SAKAGUCHI, Yuji ITO, Chikako OGAWA, Tomohiko NAKATA, Tamiko NEGORO, Kazuyoshi WATANABE, and Jun NATSUME

Department of Pediatrics, Nagoya University, Nagoya, Japan

**Objective:** Acute encephalitis with refractory, repetitive partial seizures (AERRPS) is characterized by sudden onset of refractory repetitive partial seizures and evolution to post-encephalitic epilepsy without a latent period. Although effectiveness of ketogenic diet (KD) has been reported in AERRPS, the response to the KD is variable in each patient. In this report we present 2 children with AERRPS to show the variability of the response timing to KD.

**Patients:** Patient 1 was 6-year-old girl. She started to have seizures 3 days after febrile illness. Seizures disappeared by continuous infusion of thiamylal. However thiamylal was discontinued because of skin eruption and seizures relapsed. KD was started 1 month after the onset of AERRPS. Seizures disappeared during the fasting period before starting ketogenic fomula. Patient 2 was 14-year-old girl. She started to have focal seizures at 6 days of febrile illness. Continuous thiamylal infusion resulted in cessation of seizures. However seizures relapsed after reduction of thiamylal. KD was started at 19 days after the onset of AERRPS. The patient continued to have seizures during fasting period and 3:1 ratio KD. On day 25, KD ratio was increased to 4:1 and seizures disappeared. Both patients have been free of seizures during follow-up period, but have mild intellectual disability.

**Discussion:** Several factors may cause the difference of the response to KD in these patients, such as disease severity, timing of KD induction, concurrent medication or blood concentration of ketone body. It is important to recognize the variability of the response timing to KD in evaluation of the efficacy of the treatment.

## P-23 ACUTE ENCEPHALITIS WITH REFRACTORY, REPETITIVE PARTIAL SEIZURES (AERRPS); A CLINICAL STUDY OF FIVE CHRONIC CASES

<u>Noriko SAWAURA</u>, Kazuhiro MURAMATSU, Nishiki MAKIOKA, Tomomi OGATA, Hirokazu ARAKAWA

Department of Padiatrics, Gunma University, Graduate School of Medicine, Gunma, Japan

**Background:** Acute encephalitis with refractory, repetitive partial seizures(AERRPS) is a neurologic syndrome characterized by the acquisition of extraordinary epileptogenicity, accompanied by frequent partial seizures, evolve into refractory epilepsy. In most cases, the outcome is unfavorable due to intractable epilepsy and cognitive deficits. In the present study, we report the clinical characteristics of five chronic cases with AERRPS.

**Methods & Results:** The age at onset is 5~11 years and follow-up duration of four patients excluding the one case by moving is for 5~13 years. All patients had residual epilepsy and needed two or more antiepileptic drugs. Effective antiepileptic drugs for patients with chronic phase are different from individually. The type of seizures were mainly partial seizures, they were essentially same as those in the acute phase. During initial recovery period, three patients showed a visual impairment which improved gradually in a few months. Most patients had cognitive impairment. One patient with autism had relatively mild acute phase, so he did not change in general development including the cognitive function according to the evaluation of the family. One patient who was most severe course during the acute phase showed most serious outcome. Other neurological symptoms as sequela included sleep disorder, precocious puberty and psychiatric symptom. Cranial MRI findings revealed diffuse cerebral atrophy in three cases after few months or more. Many cases were accompanied by a skull thickening, it might be due to the antiepileptic drugs for long duration.

**Conclusion:** It is considered that the course of acute phase is associated with neurological outcome. We strongly hope that the pathophysiology will be elucidated and the adequate treatment in acute phase will be established as soon as possible.

#### PATHOGENIC AGENTS DETECTED AMONG ACUTE ENCEPHALITIS AND ENCEPHALOPATHY CASES LESS THAN 5 YEARS OF AGE, JAPAN, 2011-2015.

<u>Hideo OKUNO</u>, Tomimasa SUNAGAWA, Saeko MORINO, Hiroshi SATOH, Satoru ARAI, Kazunori OISHI, Keiko TANAKA-TAYA Infectious Disease Surveillance Center, National Institute of Infectious Diseases, Tokyo, Japan

**Introduction:** Acute encephalitis/encephalopathy (AE) is a notifiable disease in Japan. Clinicians who diagnose a patient with AE are legally required to notify the case to the national surveillance system (National Epidemiological Surveillance of Infectious Disease; NESID).

**Methods:** AE cases <5 years of age reported through NESID from 2011-2015 were described by predefined age groups (<6 months, 6-11months, 1 year, and 2-4 years) and pathogen. We assessed the distribution of the pathogens detected among AE in Japanese infants.

**Results:** Among a total of 1008 case reported, 520 (51.6%) were male. 453 (44.9%) cases were reported with pathogenic agents and age distribution was as follows: 45 (10.2%) cases were <6 months, 85 (13.2%) cases were 6-11 months, 185 (33.1%) cases 1 year, and 213 (43.5%) cases 2-4 years. The most common pathogens detected were influenza virus (Flu) (132 cases, 29.1%) followed by human herpesvirus 6/7 (HHV6/7) (100 cases, 22.1%), rotavirus (RV) (57 cases, 12.6%), human enteroviruses (EV) (32 cases, 7.1%), and respiratory syncythial virus (22 cases, 4.9%). Among cases <6 months of age, herpes simplex virus (15 cases, 33.3%), EV (9 cases, 20%), and human parechoviruses (9cases, 20%) were more common relative to other groups while HHV6/7 (35 cases, 58.3%) were detected more frequently among those aged 6-11 months. In 1 year group, HHV6/7 (54 cases, 29.2%) and Flu (31cases, 16.8%) were more common pathogens. Among cases of 2-4 years, Flu (92 cases, 43.2%) and RV (35 cases, 16.4%) were major pathogens, however HHV6/7 (10 cases, 4.7%) were identified less frequently.

**Conclusion:** We found that viruses composed the majority of reported AE cases <5 years of age and the distribution of pathogenic viruses differed by age group. These findings indicate the importance of accounting for age group and pathogen when examining patients <5 years of age with AE.

#### P-25 A CASE OF SCRUB TYPHUS MENINGOENCEPHALITIS WITHOUT ESCHAR AND DIRECT EXPOSURE HISTORY

#### Young Ok KIM and Young Jong WOO

Department of Pediatrics, Chonnam National University Medical School, Gwangju, Republic of Korea

**Objective:** Scrub typhus is an infective disease caused by Orientia tsutsugamushi, showing fever, headache, myalgia, and arthralgia within 7–10 days after mite bite. Some patients with scrub typhus were reported to show central nervous system dysfunction such as altered mental status or sensorium and seizure. Eschar is an important diagnostic sign of scrub typhus, but may not be found in up to 30% of cases. We report a patient with scrub typhus meningoencephalitis, in whom diagnosis was late due to absence of eschar and indirect exposure history to mites.

**Case:** A 6-year-old boy was transferred due to altered mental status following seizures and fever from 9 days ago. He had been treated with an impression of meningitis, as cerebrospinal fluid (CSF) exam showed pleocytosis (292 cell count/mm<sup>3</sup>). CSF stain, culture, bacterial antigen test, and multiplex PCR (polymerase chain reaction) test for viruses and bacteria, stool enterovirus PCR test, and blood culture did prove no pathogen. Brain magnetic resonance imaging was normal. Electroencephalography showed dysmorphic and slow delta background activities. From the laboratory tests for fever, scrub typhus antibody was positive with titer of 1:80. Although the patient showed no eschar or direct exposure history to mites, his grandmother was treated for scrub typhus 2 weeks ago and his father helped her farming. As he often cared the patient wearing his working pants, his clothe might be a vehicle of infection. The boy was gradually recovered on clarithromycin in addition to intravenous methylprednisolone and immunoglobulin treatment and was discharged on the 14<sup>th</sup> hospital date.

**Conclusion:** As scrub typhus can be seen without eschar and can be caused by indirect exposure through contaminated clothes, scrub typhus antibody test in serum is recommended in encephalopathy or meningoencephalitis patients visiting a hospital between June and November (from rainy months to the time of harvest).

### PATTERNS OF BRAIN LESIONS IN NEONATES WITH HERPES SIMPLEX ENCEPHALITIS

<u>Hiroyuki KIDOKORO</u><sup>1)</sup>, Chikako OGAWA<sup>1)</sup>, Yuji ITO<sup>1)</sup>, Atsuko OHNO<sup>1)</sup>, Yu OKAI<sup>1)</sup>, Tomohiko NAKATA<sup>1)</sup>, Yoko SAKAGUTI<sup>1)</sup>, Shinji SAITOH<sup>2)</sup>, Akihisa OKUMURA<sup>3)</sup>, Jun NATSUME<sup>1)</sup>

- <sup>1)</sup> Department of Pediatrics, Nagoya University Graduate School of Medicine, Nagoya, Japan
- <sup>2)</sup> Department of Pediatrics and Neonatology, Nagoya City University Graduate School of Medicinal Sciences, Nagoya, Japan
- <sup>3)</sup> Department of Pediatrics, Aichi Medical University, Nagakute, Japan

**Objective:** To report a classification for brain lesions in neonatal herpes simplex encephalitis (HSE), and secondly investigate the association between pattern of brain lesions, clinical variables and neurodevelopmental outcome.

**Methods:** A multicenter retrospective study was performed in neonates diagnosed with HSE between 2009 and 2014. MR images, including diffusion-weighted images were obtained in the acute and chronic phase.

**Results:** Three main patterns of brain injury could be defined based on characteristic MRI findings in 10 the 13 infants (77%). The inferior frontal/temporal pole pattern was noted in five (38%) patients. The watershed distribution pattern was present in six (46%) patients. Four (31%) infants had the corticospinal tract pattern. No significant association was found between any brain lesion pattern and sex, country, viral type or viral load. However, the corticospinal tract pattern was significantly associated with motor impairment (p=0.046) and the inferior frontal/temporal pole pattern with West syndrome (p=0.028).

**Conclusion:** Three patterns of brain lesion can be recognized in neonatal HSE. Pattern recognition can improve prediction of neurodevelopmental outcome.

#### P-27 BARBITURATE COMA THERAPY FOR CHILDREN WITH ACUTE ENCEPHALOPATHY

<u>Yusuke ISHIDA<sup>1</sup></u>, Kazumi TOMIOKA<sup>2</sup>, Tsukasa TANAKA<sup>1</sup>, Masahiro NISHIYAMA<sup>2</sup>, Kyoko FUJITA<sup>1</sup>, Daisaku TOYOSHIMA<sup>1</sup>, Azusa MARUYAMA<sup>1</sup>, Hiroaki NAGASE<sup>2</sup>, Hiroki TAKEDA<sup>3</sup>, and Yoshiyuki UETANI<sup>3</sup>

- <sup>1)</sup> Department of Neurology, Hyogo Prefectural Kobe Children's Hospital, Kobe, Japan
- <sup>2)</sup> Department of Pediatrics, Kobe University Graduate School of Medicine, Kobe, Japan
- <sup>3)</sup> Department of Emergency and Critical Care Medicine, Hyogo Prefectural Kobe Children's Hospital, Kobe, Japan

**Objectives:** Barbiturate coma therapy (BCT) was commonly used for refractory status epilepticus (RSE). However, BCT for acute encephalopathy has yet to be reported. The aim of this study was to investigate the managerial approach and safety of BCT using thiamylal for acute encephalopathy. Specifically, we conducted the study to reveal the adequate dose of thiamylal and time necessary to achieve a burst suppression pattern (BSP) based on continuous electroencephalography.

**Methods:** We reviewed the medical records of children who were treated with BCT for acute encephalopathy between 2012 and 2015. We included children who: 1) were admitted to the pediatric intensive care unit at Kobe Children's Hospital because of convulsion or impaired consciousness with fever, 2) exhibited RSE and/or prolonged neurological abnormality and/or aspartate aminotransferase levels >90 IU/l within 6 h of onset, 3) were treated with BCT using thiamylal. We investigated the dose and time to achieve BSP, and complications at induction of BCT. According to the hospital-based protocol, BCT was combined with targeted temperature management and mechanical ventilation with intubation, thiamylal was administered by 1-2mg/kg until identification of BSP on continuous electroencephalography, and vasopressor was used to keep mean blood pressure at more than 50-70mmHg.

**Results:** Subjects consisted of 49 children with a median (range) age of 35 (6-137) months. The median total dose of thiamylal to achieve BSP was 27 (7-67) mg/kg. The median time adequate to achieve BSP was 115 (4-343) minutes. Although all patients needed one or more vasopressors, BCT was completed with all patients except one who showed severe hypotension. No other severe adverse events related to thiamylal were observed.

**Conclusions:** To the best of our knowledge, this is the first study to clarify the specific regimen and safety using thiamylal to achieve BSP for children with acute encephalopathy.

### P-28

#### STATUS EPILEPTICUS IN INFLUENZA VIRUS INFECTION AFTER INTRAVENOUS FOSPHENYTOIN ADMINISTRATION WITHOUT PRECEDING BENZODIAZEPINE

<u>Yuji SUGAWARA</u>, Saori AMANO, Eriko ADACHI, Takeshi SATO, Tomiyuki HISHIYAMA, Shigeru TAKISHIMA, Kentaro MIKAMI, Naoko ISHIBASHI, Takeshi HASEGAWA, and Sirou TSUCHIYA

Department of Pediatrics, Soka Munincipal Hospital, Soka, Japan

**Introduction:** Intravenous fosphenytoin (fosPHT) is widely used for febrile convulsive status epileptics (SE) or febrile seizure clusters in children. It is one of the second-line drugs when short-acting benzodiazepines (BZPs) fail to terminate SE. Seizure aggravation by phenytoin or fosPHT can develop in subjects with idiopathic generalized epilepsy and several genetically defined epilepsy, for example Dravet syndrome, but similar observation was not reported in febrile convulsive SE of previously healthy children.

**Case Series:** Since 2012, we administered fosPHT for 14 children with febrile seizure cluster. While fosPHT followed BZPs in 8 subjects, including 1 with influenza virus infection (Flu), fosPHT was the 1st anticonvulsant in 6, including 4 with Flu. In 3 of 4 children with Flu treated by fosPHT without preceding BZPs, SE subsequently developed. The three patients (2, 4, and 6 years-old male respectively) were previously healthy. The preceding seizures were uncomplicated but repeated twice at an interval of 4-12 hours. Between the seizures neither drowsiness nor neurological deficit was seen. To abrogate seizure cluster, 22.5mg/kg fosPHT was administered intravenously, but 0.5-3.0 hours later convulsive seizure relapsed. The relapsed seizures were refractory to BZPs and progressed to SE, eventually terminated by intravenous phenobarbital (seizure duration 20-30 minutes). The subjects remained comatose and electroencephalogram revealed diffuse high-voltage slow waves. All patients were treated by high-dose intravenous methylprednisolone, and the consciousness level gradually recovered without seizure recurrence.

**Discussion:** In association with Flu, after particular use of fosPHT, the three patients developed SE that is generally considered to infrequently follow uncomplicated febrile seizures without impaired consciousness. Furthermore the temporal relationship was distinct between fosPHT administration and SE onset. These observations suggest that fosPHT without preceding BZPs can trigger SE in some settings. To elucidate the underlying mechanisms, further investigation is necessary including serum level of PHT.

## P-29 TWO UNIQUE CASES OF PYRIDOXAL PHOSPHATE-RESOPNSIVE INFANTILE EPILEPTIC ENCEPHALOPATHIES

<u>Yoshiyuki HANAOKA</u>, Takushi INOUE, Takashi SHIBATA, Tomoyuki AKIYAMA, Makio OKA, Harumi YOSHINAGA, and Katsuhiro KOBAYASHI

Department of Child Neurology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences and Okayama University Hospital, Okayama, Japan

**Introduction:** Pyridoxal phosphate (PLP) is among effective treatments for infantile epileptic encephalopathies including West syndrome (WS) and Ohtahara syndrome (OS). We report unique cases of such disorders that were associated with structural brain pathology and dramatically responded to PLP.

**Case 1:** The patient is a boy who developed West syndrome. At 3 months of age, he was involved in an automobile accident and had subarachnoid hemorrhage, a skull fracture and a brain contusion. He began to have epileptic spasms in series, and the EEG showed hypsarrhythmia at 6 months of age. Although his spasms disappeared and EEG improved soon after the start of PLP treatment, spasms relapsed and EEG worsened after an operation for a growing skull fracture performed at 7 months of age. Administration of sodium valproate (VPA) was not effective. Increase of the dose of PLP up to 40mg/kg/ day with discontinuation of VPA was effective to suppress spasms with associated EEG improvement. The patient has been seizure-free since then until now at 5 years of age.

**Case 2:** A boy had OS: he developed epileptic spasms in series at 1 month of age, and the EEG showed a suppression-burst pattern dominant over the right hemisphere during both wakefulness and sleep. He had a focal cortical dysplasia involving the right frontal lobe. He did not show myoclonic seizures. Spasms disappeared and EEG improved dramatically 2 weeks after the start of PLP treatment, when the dose of PLP was 18mg/kg/day.

**Conclusion:** PLP is occasionally effective even for epileptic encephalopathies with structural brain pathology. PLP is worth a trial for severe infantile epilepsies.
# WEST SYNDROME- A SINGLE CENTRE 5-YEAR REVIEW FROM SINGAPORE

P-3(

<u>Hian-Tat ONG</u><sup>1), 2)</sup>, Karen JL LIM<sup>2)</sup>, Furene SJ Wang<sup>1)</sup>, Poh Sim LOW<sup>1), 2)</sup>, Stacey KH TAY<sup>1), 2)</sup>

- <sup>1)</sup> Khoo Teck Puat National University Children's Medical Institute, National University Hospital, National University Health System, Singapore
- <sup>2)</sup> Department of Pediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

**Objective:** To review the cause, treatment and progress of infants who were recently referred to our center for the management of West syndrome.

**Method:** We reviewed the clinical records and video-EEGs of patients below 12 months of age who develop West syndrome (a form of infantile epileptic encephalopathy) in a 5-year period from 2011 to 2015 inclusive. All infants had EEGs showing hypsarrhythmia and/or infantile spasms recorded for the diagnosis.

**Results:** A total of 22 infants had confirmed diagnosis of West syndrome. There were 18 symptomatic patients and the etiologies were: lissencephaly (2), tuberous sclerosis (2), other forms of cerebral malformation or atrophy (5), intrauterine infection (1), post intrauterine stroke (1), inborn errors of metabolism (1), post CNS infection (3), presumably genetic (1), Budd Chiari syndrome (1) and unknown (1). There were 4 infants with normal neurodevelopment prior to the onset of the infantile spasms, and were thus classified as idiopathic. Most patients had treatment with steroid or vigabatrin as the anti-epileptic drug (AED) of choice. Various other AEDs used included topiramate, valproic acid and clonazepam. On long term follow-up, most patients had developmental delay, even if the infantile spasms were controlled.

**Conclusions:** As expected, most patients with West syndrome in our series were symptomatic cases. The long term prognosis remains guarded after successful treatment of West syndrome, even in the patients who were classified as idiopathic.

# P-31 THE EFFECT OF STEROID PULSE THERAPY ON A CASE OF DRAVET SYNDROME

<u>Takako FUJITA</u><sup>1)</sup>, Hiroshi IDEGUCHI<sup>1)</sup>, Eri WATANABE<sup>1)</sup>, Yuko TOMONOH<sup>1)</sup>, Yukiko IHARA<sup>1)</sup>, Takahito INOUE<sup>1)</sup>, Yukitoshi TAKAHASHI<sup>2)</sup>, Shinichi HIROSE<sup>1)</sup>, Sawa YASUMOTO<sup>3)</sup>

<sup>1)</sup> Department of Pediatrics, School of Medicine, Fukuoka University

<sup>2)</sup> Shizuoka Institute of Epilepsy and Nuerological Disorders

<sup>3)</sup> Center of medical education, School of medicine. Fukuoka University

**Background:** Dravet syndrome is an epileptic syndrome presenting with various types of seizures that begin in the first year of life and may result in intellectual impairment. Recently, the occurrence of acute encephalopathy in children with Dravet syndrome has been reported.

**Purpose:** To examine the effect of steroid pulse therapy on a Dravet syndrome patient who exhibited encephalopathy.

**Methods And Results:** This girl first had a convulsive status with fever at age 11 months. She exhibited both partial and generalized seizures and sometimes, when overheated, as with a fever or in a hot bath, she had convulsive status. Several antiepileptic drugs were not effective. When three years old, she was diagnosed with Dravet syndrome, mental retardation, and autism with hyperkinesia. She did not have *de novo* mutations in *SCN1A* or *PCDH19*. At 5, she showed fever, seizure clusters, and a slight disturbance of consciousness. EEG revealed persistent high voltage slow waves with irregular spike-and-wave complexes. She acquired anti-GluR antibodies in cerebrospinal fluid. We diagnosed encephalopathy and treated her with steroid pulse therapy. After steroid pulse therapy, she recovered consciousness and her hyperkinetic and aggressive behaviors improved; EEG showed her high voltage slow waves had disappeared. She had no convulsive status after steroid pulse therapy and her seizures decreased.

**Conclusions:** In this case, steroid pulse therapy was an effective treatment in encephalopathy of Dravet syndrome. The case also suggests that the immune system might be participated with aggravation of seizures of Dravet syndrome.

# EPILEPTIC ENCEPHALOPATHY MARKER OF INBORN ERRORS OF METABOLISM

**P-3** 

<u>Ashok GUPTA</u>, Priyanshu MATHUR, Kamlesh AGARWAL SMS Medical College, Jaipur, India

**Objective:** Epileptic encephalopathy can be induced by inborn metabolic defects that may be rare individually but in aggregate represent a substantial clinical portion of child neurology. These may present with various epilepsy phenotypes including refractory neonatal seizures, early myoclonic encephalopathy, early infantile epileptic encephalopathy, infantile spasms, and generalized epilepsies which in particular include myoclonic seizures. There are varying degrees of treatability, but the outcome if untreated can often be catastrophic. The importance of early recognition cannot be overemphasized. Thus, the study has been done with the objective of evaluating all new born & infants presenting with unexplained encephalopathy for possible inborn errors of metabolism.

**Method:** The study is a hospital based prospective non interventional observational in nature. All new born and infants presenting with unexplained seizures and encephalopathy during the period of Jan 1, 2015 to Dec 31, 2015 were enrolled in the study. An informed consent was taken from the guardians and a screening for metabolic errors was conducted and for patients suggesting a positive possibility were subjected to a confirmatory test.

**Results:** 262 children of which 140 new borns were evaluated for inborn errors of metabolism. The following disorders of metabolism were identified – Maple Syrup Urine Disease, Homocystine Urea, Galactosemia, Lysosomal Storage Disorders, Tay Sachs & Alexandra Disease.

**Conclusion:** Epileptic Encephalopathies represent a challenging area of pediatric neurology and epilepsy and have a broad differential diagnosis. There are protean inborn errors of metabolism which may lead to epileptic encephalopathies. This study one of the first in the state clearly identifies the prevalence of metabolic errors which were not thought previously. It is important to diagnose them as they have various degrees of treatability at present, with some requiring prompt diagnosis and intervention to avoid otherwise catastrophic outcomes.

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# P-33 DRUGS INDICATED FOR MITOCHONDRIAL DYSFUNCTION AS TREATMENTS FOR ACUTE ENCEPHALOPATHY WITH ONSET OF FEBRILE CONVULSIVE STATUS EPILEPTICS

<u>Taku OMATA</u><sup>1)</sup>, Katsunori FUJII<sup>2)</sup>, Jun-ichi TAKANASHI<sup>3)</sup>, Kei MURAYAMA<sup>4)</sup>, Masaki TAKAYANAGI<sup>4)</sup>, Kaori MUTA<sup>1)</sup>, Kazuo KODAMA<sup>1)</sup>, Yukiko IIDA<sup>1)</sup>, Yoshimi WATANABE<sup>1)</sup>, Naoki SHIMOJO<sup>2)</sup>

- <sup>1)</sup> Division of Child Neurology, Chiba Children's Hospital, Chiba, Japan
- <sup>2)</sup> Department of Pediatrics, Chiba University Graduate School of Medicine, Chiba, Japan
- <sup>3)</sup> Department of Pediatrics, Tokyo Women's Medical University Yachiyo Medical Center, Yachiyo, Japan
- <sup>4)</sup> Division of Metabolism, Chiba Children's Hospital, Chiba, Japan

**Objective:** Acute encephalopathy with onset of febrile convulsive status epilepticus can be difficult to distinguish from febrile convulsive status epilepticus and often results in severely handicapped patients. One significant etiology of acute encephalopathy is depletion of energy due to decreased mitochondrial function. In mitochondrial diseases, various vitamins and coenzymes have been used clinically based on their effects on energy shortage and oxidative stress, and their effectiveness has been reported at high doses. Therefor this study aimed to examine the efficacy of combination of vitamin B1, vitamin C, biotin, vitamin E, coenzyme Q10, and L-carnitine as "mitochondrial drug cocktails" in the treatment of acute encephalopathy.

**Methods:** We studied the efficacy of drugs indicated for mitochondrial dysfunction in the treatment of 21 patients with acute encephalopathy with onset of febrile convulsive status epilepticus at our hospital from January 2006 to December 2014.Among them, 11 patients had been treated with a mitochondrial drug cocktail consisting of vitamin B1, vitamin C, biotin, vitamin E, coenzyme Q10, and L-carnitine (prescription group) and 10 patients were not treated with the cocktail (non-prescription group). We retrospectively reviewed age, trigger, clinical form, treatment start time, and sequelae. Clinical formwas classified into a biphasic group presenting acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) and a monophasic group. Sequelae were classified as (A) no sequelae group or (B) sequelae group, and differences in the interval between diagnosis and treatment were also evaluated.

**Results:** The sequelae were not different between the mitochondrial drug cocktail prescription and non-prescription groups, but significantly better in the group administered the mitochondrial drug cocktail within 24 h (P = 0.035).

**Conclusion:** We expect that early treatment with a mitochondrial drug cocktail could prevent sequelae in acute encephalopathy with onset of febrile convulsive status epilepticus.

# INCREASED FRACTIONAL ANISOTROPHY, A PARAMETER OF DIFFUSION TENSOR IMAGING, REFLECTS REVERSIBILITY OF ACUTE ENCEPHALOPATHY

<u>Shihoko KIMURA-OHBA</u><sup>1)</sup>, Yi YANG<sup>1)</sup>, Jeffrey THOMPSON<sup>1)</sup>, Tomonori KIMURA<sup>2)</sup>, Yirong YANG<sup>3)</sup>, Laurel O SILLERUD<sup>3)</sup> and Gary A ROSENGERG<sup>1)</sup>

<sup>1)</sup> Department of Neurology, Health Science Center, University of New Mexico, Albuquerque, USA

<sup>2)</sup> Department of Molecular Genetics and Microbiology, University of New Mexico, Albuquerque, USA

<sup>3)</sup> BRaIN Imaging Center, University of New Mexico, Albuquerque, USA

[Introduction] The diffusion tensor imaging (DTI) has recently moved into clinical practice, with particular attention being paid to measurements of the fractional anisotropy (FA) of water diffusion in the brain. Brain vasogenic edema, involving disruption of the blood-brain barrier (BBB), is a common pathological condition in several neurological diseases, with a heterogeneous prognosis. It is sometimes reversible, as in posterior reversible encephalopathy syndrome (PRES), but often irreversible as seen in lesions of vascular cognitive impairment. Currently, our clinical tools cannot distinguish the reversibility of these diseases. Here we aimed to find the MRI/DTI signals which can delineate the reversibility of brain vasogenic edema.

[Experimental Design] Spontaneously hypertensive rats-stroke prone (SHRSP) were treated with high-dose cyclosporine A to induce encephalopathy mimicking PRES. The recovery from the encephalopathy was achieved by the cessation of cyclosporine A. The extent and recovery of neurological symptoms and brain lesion were monitored by neurological score, behavioral tests, and MRI. BBB leakage was histologically confirmed.

[Results] SHRSP demonstrated PRES-like acute encephalopathy in response to highdose cyclosporine A treatment; the deteriorating neurological symptoms and worsening scores in behavioral tests, which were seen in acute phase, disappeared after recovery by cessation of cyclosporine A. In the acute phase of encephalopathy, the FA and apparent diffusion coefficient increased in areas with IgG leakage. This increase of FA occurred in the absence of demyelination: fluid leakage into the myelinated space increased the axial, but not the radial, diffusivity, resulting in the increased FA. This increased FA returned to pre-encephalopathy values in the recovery phase.

[Conclusion] We proved that increased FA is associated with the reversibility of vasogenic edema. Our results highlight the importance of the FA increase as a marker for the reversibility of brain edema. Measurements of FA has the potential to delineate the brain areas for which recovery is possible.

Key words (5) blood-brain barrier (BBB) brain vasogenic edema posterior reversible encephalopathy syndrome (PRES) fractional anisotropy (FA) diffusion tensor imaging (DTI)

# P-35 EPILEPTIC ENCEPHALOPATHY WITH CONTINUOUS SPIKE AND WAVE DISCHARGES DURING SLEEP IN A GIRL WITH ATYPICAL ABSENCE

Ying-Chao CHANG<sup>1)</sup>, Chao-Ching HUANG<sup>2)</sup>

<sup>2)</sup> Department of Pediatrics, National Cheng Kung University Hospital, Tainan City, Taiwan and Department of Pediatrics, Taipei Medical University, College of Medicine, Taipei, Taiwan

**Objectives**: Epileptic encephalopathy with continuous spikes and waves during slow sleep (EECSWS) is characterized by epilepsy, cognitive or behavioral impairment, and electroencephalographic (EEG) abnormality of CSWS. A large proportion of patients presenting with EECSWS are children with symptomatic epilepsy associated with different types of brain lesions. Here we report a girl with atypical absence epilepsy evolving into EECSWSS.

**Case Report:** A 7-year-old girl had frequent staring episodes since the age of 5. She has no family history of epilepsy or febrile seizures. Her neurological examination and blood test revealed no abnormality. Generalized spike and wave discharges (2.5-3 Hz) were detected both when awake and sleep with normal background activity. Absences decreased with 30 mg/Kg/day valproate (VPA) therapy. One episode of left hand clonic movements followed by transient left hand weakness was noted after adding on lamotrigine (0.5 mg/Kg/day). Frequent eyelid myoclonia, myoclonic jerks, nodding and atonic seizures developed even after withdrawing lamotrigine and adding on clonazepam, levetiracetam or zonisamide, and ketogenic diet. Occasional generalized tonic seizures were noted. Her cerebrospinal fluid examinations and cranial MR image studies showed normal. Her cognition and attention deteriorated and the EEG revealed CSWS. Steroid was used and she had marked improvement in seizure control and neurocognition.

**Conclusions:** ESCSWS occur in different types of childhood epilepsy, generally accompanied by seizures and neuropsychological decline. Prolonged sleep EEG studies should be utilized more frequently for children with epilepsy reporting cognitive or behavioral problems, even in unsuspected cases with initial "benign" epilepsy such as absence.

<sup>&</sup>lt;sup>1)</sup> Department of Pediatrics, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan

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### 医療施設(順不同)

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