The 20th Annual Meeting of Infantile Seizure Society

International Symposium on Neonatal Seizures: Deepening Insights into Developmental Brain Injury

31 May(Fri.) - 1 June(Sat.) 2019

Akihisa Okumura, M.D.
Department of Pediatrics, Aichi Medical University

Venue : Nagoya Congress Center

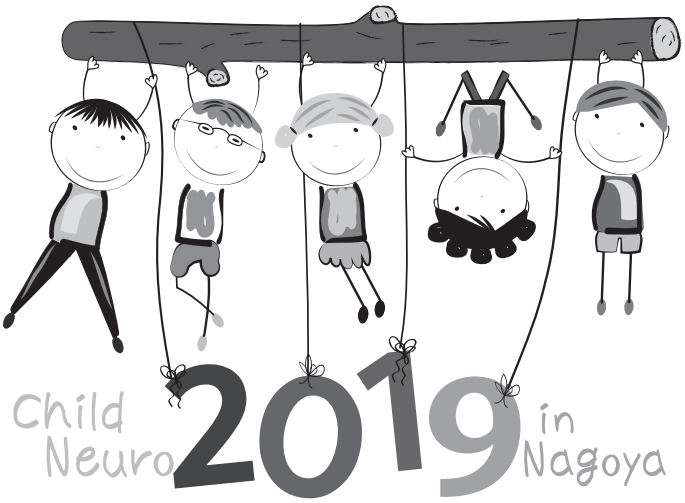
1-1 Atsuta-nishimachi, Atsuta-ku, Nagoya 456-0036 TEL:+81-52-683-7711 FAX:+81-52-683-7777

Program & Abstracts

The 20th Annual Meeting of Infantile Seizure Society

International Symposium on Neonatal Seizures: Deepening Insights into Developmental Brain Injury

PROGRAM & ABSTRACTS



31 May(Fri.) - 1 June(Sat.) 2019
Nagoya Congress Center

Organizer	Infantile Seizure Society (ISS)
Endorsement from	The Japan Epilepsy Society
	The Japanese Society of Child Neurology
	Japan Foundation for Pediatric Research

CONTENTS

Message from the President of ISS2019

Akihisa Okumura, M.D.
Department of Pediatrics, Aichi Medical University

Dear Friends and Colleagues：

It is a great honor for me to hold the 20th Annual Meeting of Infantile Seizure Society (ISS) in Nagoya as the joint meeting with the 61st Annual Meeting of the Japanese Society of Child Neurology. On behalf of the organizing committee, we offer a warm welcome to all of you.

The main theme of the ISS2019 meeting is “Neonatal Seizures: Deepening Insight into Developmental Brain Injury”. It is not always easy for pediatric neurologists to cooperate with neonatologists. Pediatric neurologists rarely go into NICU and a majority of neonatologists seem not very interested in neurology. As a result, the problems of neonatal brain fall into the gap between pediatric neurologists and neonatologists. In order to solve problems in neonatal brain, synergy between pediatric neurology and neonatology is essential. We hope that many neonatologists as well as pediatric neurologists will participate in the ISS2019 meeting, and that this meeting will be a great help to their collaboration.

As all of you know, the founder of ISS is Prof. Yukio Fukuyama. We believe that the founder of neonatal neurology in Japan is Prof. Kazuyoshi Watanabe, a great mentor of us. His tremendous works on neonatal EEG spread from Nagoya and its surrounding cities. Nagoya is located at the center of Japan and has also been a center of neonatal neurology in Japan. Nagoya and its surrounding cities have historical heritage and are now growing to be sophisticated. Ieyasu Tokugawa, who opened the Edo shogunate in 1603 and laid the foundation for prosperity in Japan, was originally a small feudal load in Okazaki city located near Nagoya. The culture of Nagoya is different from that of Tokyo or Kyoto and will arouse your interest. The access to Nagoya is easy from all over the world. We are looking forward to participation of you to the ISS2019 meeting and having a hot and fruitful discussion with each other.

奥村彰久

Akihisa Okumura, M.D.
President, the 20th Annual Meeting of Infantile Seizure Society
Department of Pediatrics, Aichi Medical University

GENERAL INFORMATION

1. Main topics

Neonatal seizures, neonatal brain injuries, neurophysiology, structural and functional neuroimaging, genetics, diagnosis of neonatal seizures, seizure semiology, neonatal neuroprotection, antiepileptic treatment, hypothermia, automated seizure detection, fetal ultrasonography, and others

2. Target attendees

Pediatricians, neonatologists, neurologists, epileptologists, neurosurgeons, basic and clinical researchers who are interested in epilepsy, neonatal care, and neonatal neuroprotection

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 temperature in late May can be slightly on the higher side but getting cool day by day in Nagoya. Consider bring light clothes and a jacket since meeting room temperatures and personal comfort levels vary. Average temperature in June in Nagoya: Average 23.4 °C, Highest 28.1 °C, Lowest 19.6 °C

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 ISS2019 will be prepared for all participants. To Japanese colleagues, authorized CME units will be rewarded by three societies as following CME Points.

Society	Attendance	Authorship	
		Presenter	Co-author
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 (2018/10/9~2019/4/30)	Late Registration (2019/5/1~2019/5/23)	On-site Registration (2019/5/31~2019/6/1)
Members	JPY 22,000	JPY 26,000	JPY 30,000
Non-members	JPY 26,000	JPY 30,000	JPY 34,000
Paramedic / Resident / Student*	JPY 11,000		
Accompanying Person	Free		
Grand Social Party	Free		

*Copy of official documents such as a students identification or a certificate will be required.
Postgraduate students will not be included in "student"
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 for both the 20th Annual Meeting of Infantile Seizure Society and the 61st Annual Meeting of the Japanese Society of Child Neurology
2. Online proceeding Downloading App of The 61st Annual Meeting of Japanese Society of Child Neurology Password:jscn2019
3. Opening ceremony, Closing ceremony, Grand Social Party
4. Luncheon seminar and Lunch Services
5. Congress bag with program and related information and Congress badge

【 Accompanying Persons 】
Registered accompanying persons are entitled for the followings:
1. Opening ceremony, Closing ceremony, Grand Social 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: Thursday, May 30 11:30-16:00
Day 2: Friday, May 31 7:30-19:00
Day 3: Saturday, June 1 7:30-17:30
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 Social Party
Date: Saturday, June 1 19:00-21:00
Venue: Port of Nagoya Public Aquarium
(1-3 Minato-Machi, Minato-ku, Nagoya 455-0033 Japan / Tel 81-52- 654-7080)
Registration Fee: Free of charge

5. Conference Venue

Nagoya Congress Center
1-1 Atsuta-nishimachi, Atsuta-ku, Nagoya 456-0036 Japan
Access: http://www.nagoya-congress-center.jp/en/

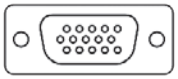
6. Conference Program and Abstracts

Price: 1,000 JPY

INSTRUCTIONS FOR ORAL AND POSTER PRESENTATIONS

Instructions for Invited Speakers and Oral Speakers in the Abstract 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 at Century Foyer (2F, Bldg. 1, Nagoya Congress Center).
4. We accept slide file attached with your name on, prepared by Microsoft Office PowerPoint 2010, 2013 and 2016 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.



D-Sub 15 pin

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 Abstract Sessions 1 and 2 are requested to adhere strictly to 7 min for presentation and 3 min for discussion (total 10 min). The time-keeper alert you to the remaining and termination time of the presentation.

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.

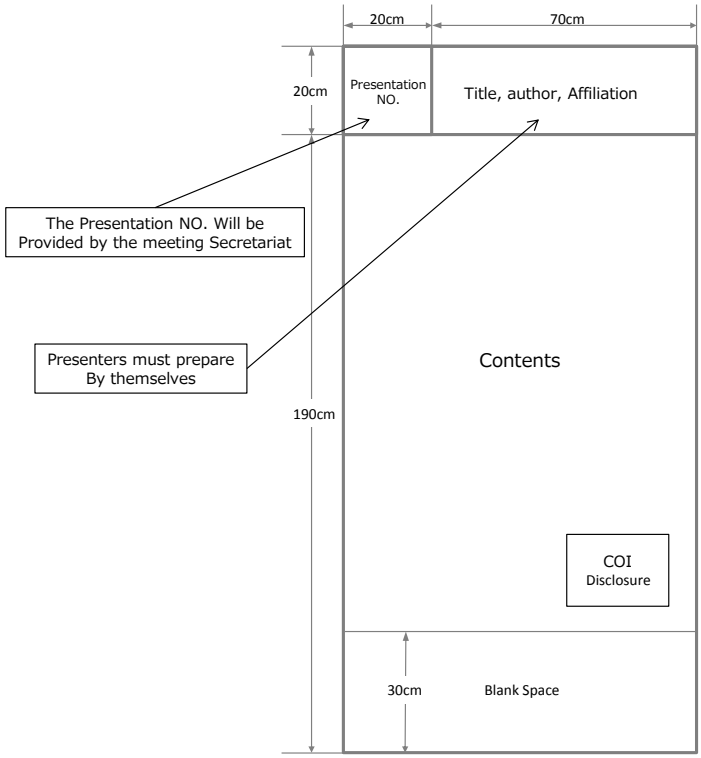
Next Chairpersons and Next Speakers

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

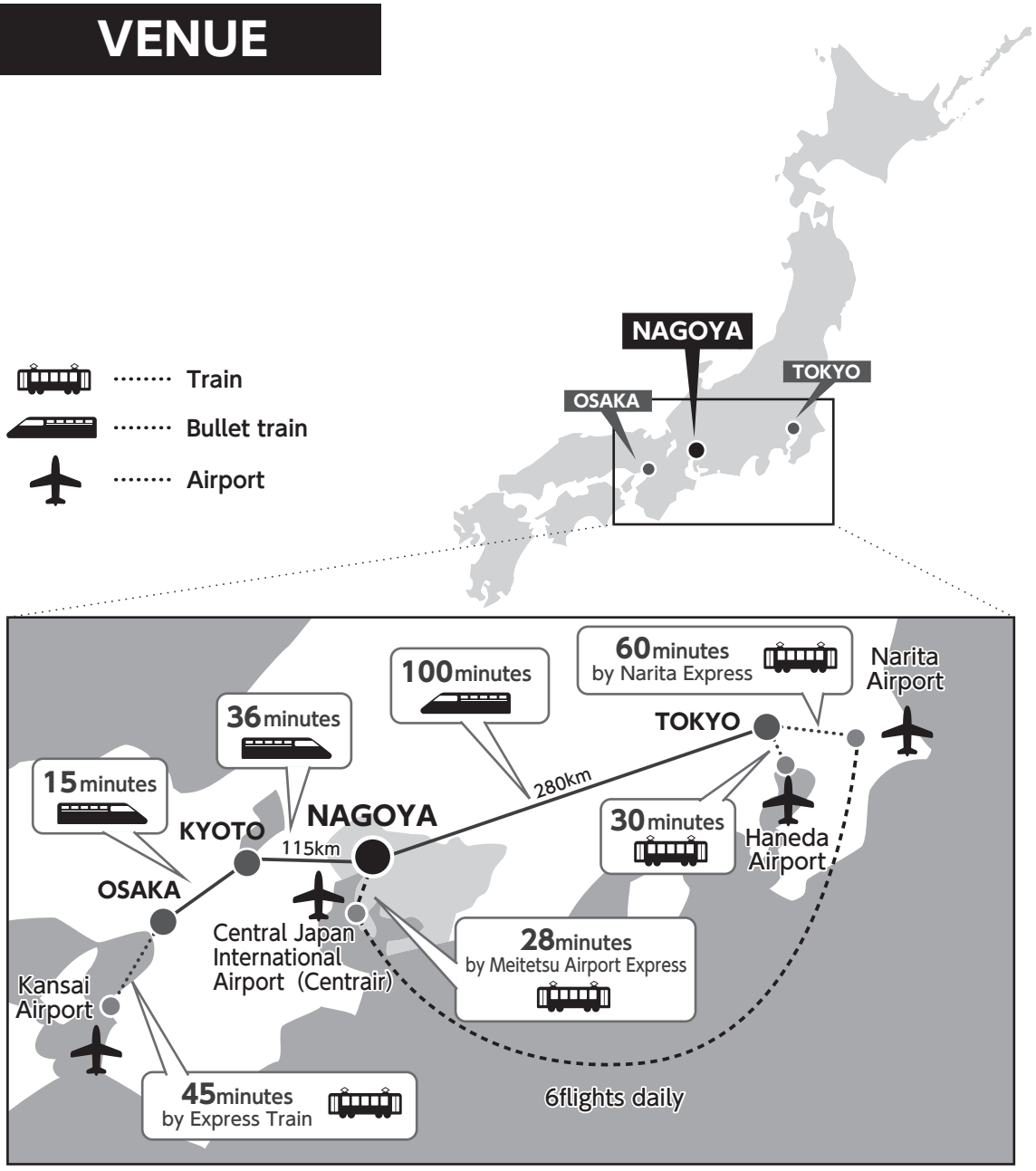
Please be seated 15 minutes prior to your presentation/session.

Instructions for the Poster Sessions

1. The Poster Sessions is held in the Poster Room at Event Hall.
2. All Posters should be set up from 8:30 to 11:30 on May 31, exhibited from 11:30 to 17:00 and removed from 18:30 to 19:00. Posters exhibited after 17:00 on June 1 shall be removed and may be discarded by the staff members of ISS2019.
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 from17:00 to 18:00 on May 31. Each speaker is requested to stay in front of his/her poster for discussion during the Poster Sessions.
5. Conflict of interest (COI) should be shown in the poster.



VENUE



From "Centrair" Central Japan International Airport

Taxi
about ¥15,000

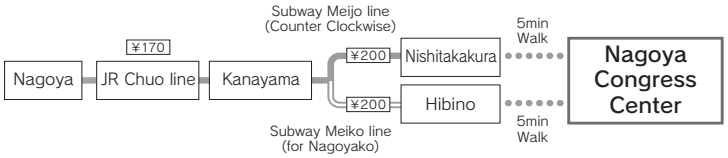
Centrair — about 40min. — Nagoya Congress Center

Subway + Meitetsu Kuko(airport)Line

Centrair — μSKY limited express about 30min. ¥1,170 — Kanayama — Subway ¥200 — Hibino (Meiko line) / Nishi Takakura (Meijo line) — 5min. by walk — Nagoya Congress Center

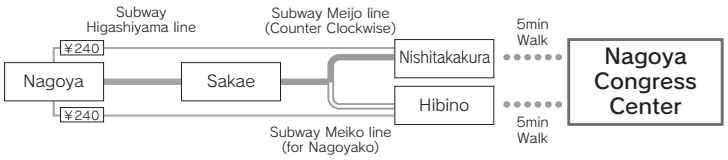
●Nagoya station to the venue via Kanayama station

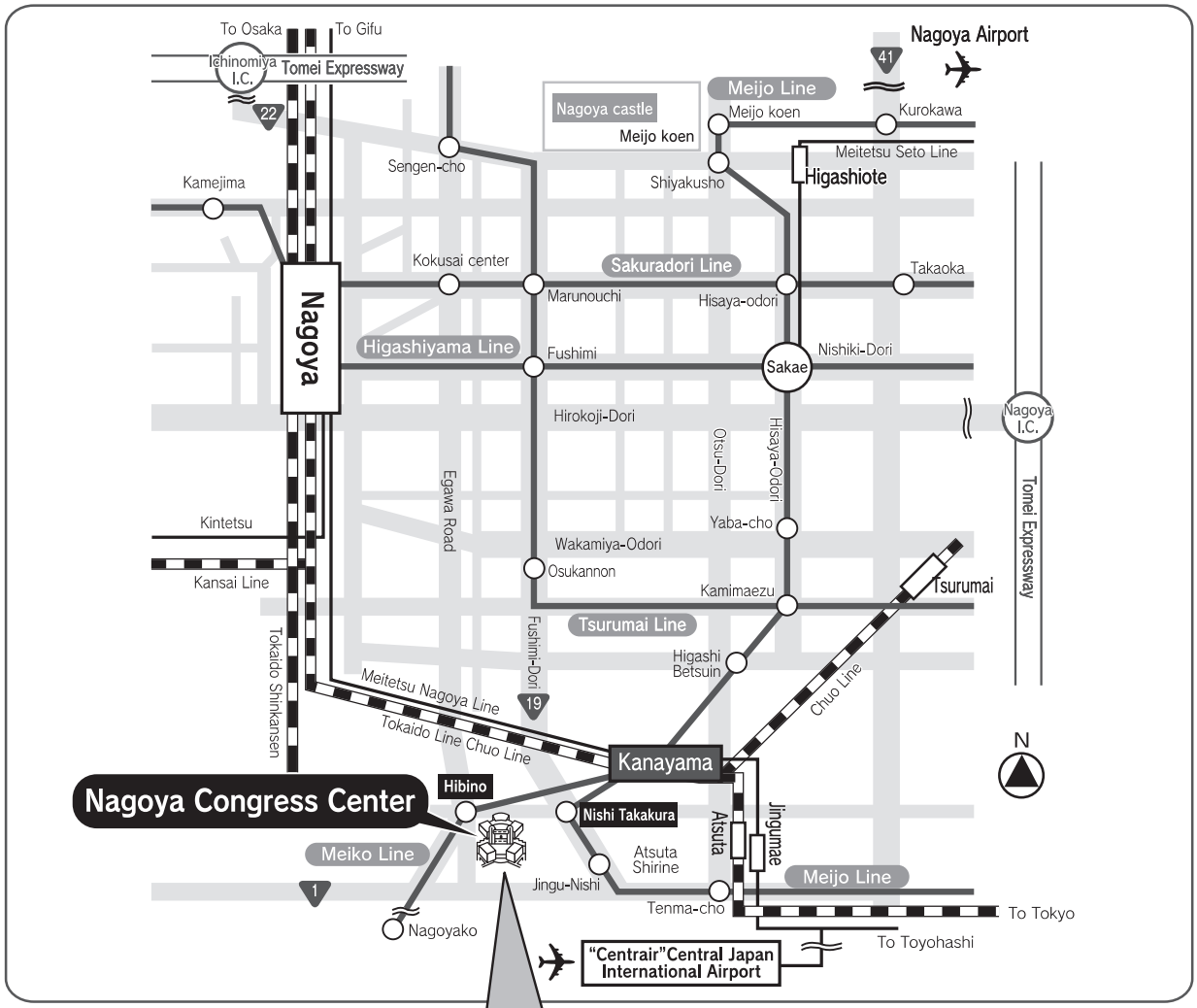
From Nagoya station, take JR "Chuo line" to Kanayama station then change to subway either Nishitakakura(Exit2) or Hibino station (Exit1). The venue will be 5 minutes walk from both stations.



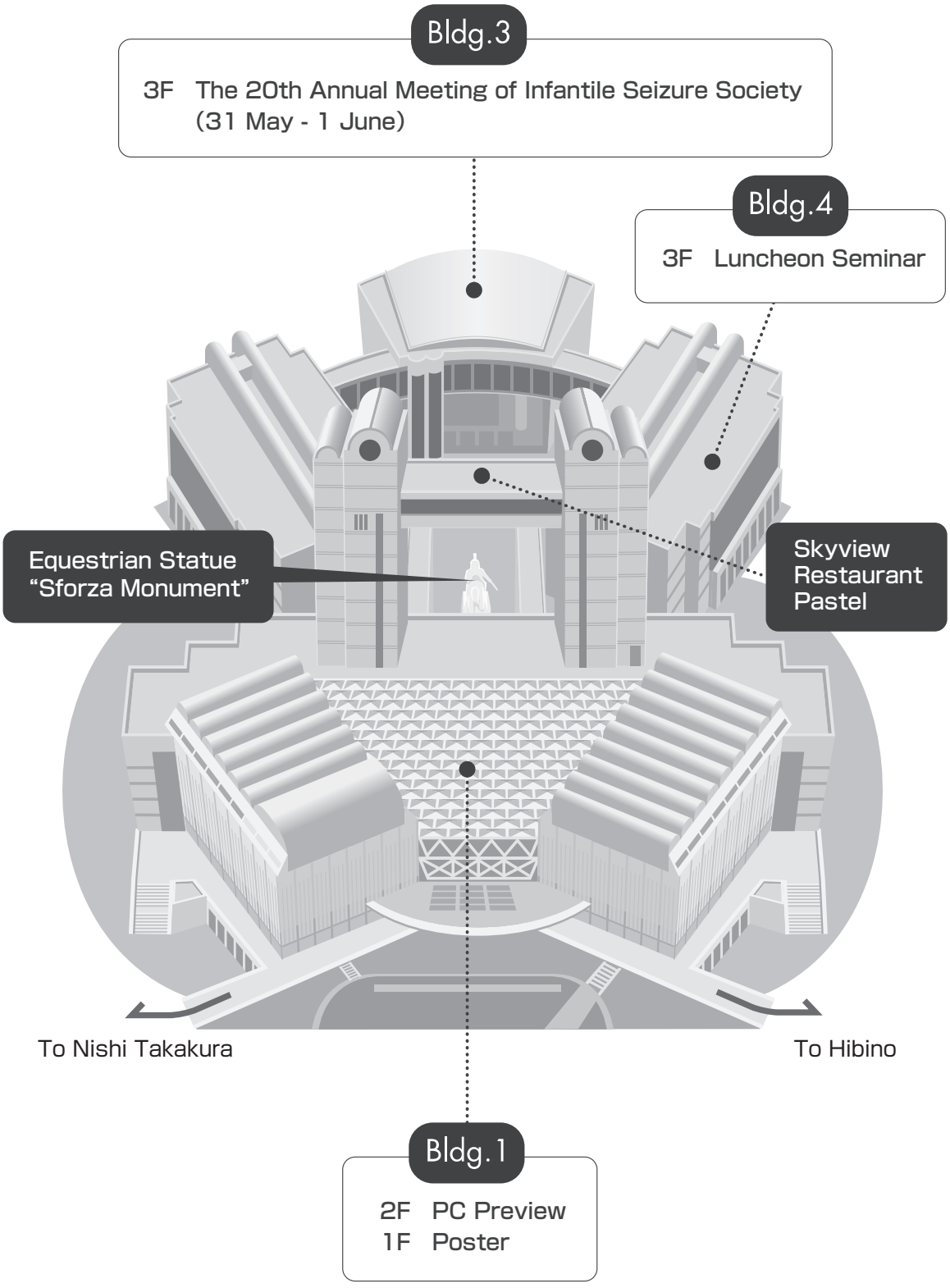
●Nagoya station to the venue via Sakae station

From Nagoya station, take subway Higashiyama line to Sakae station then change to subway at Kanayama station to either Nishitakakura(Exit2) or Hibino station (Exit1). The venue will be 5 minutes walk from both stations.





FLOOR PLAN for the CONGRESS ISS2019



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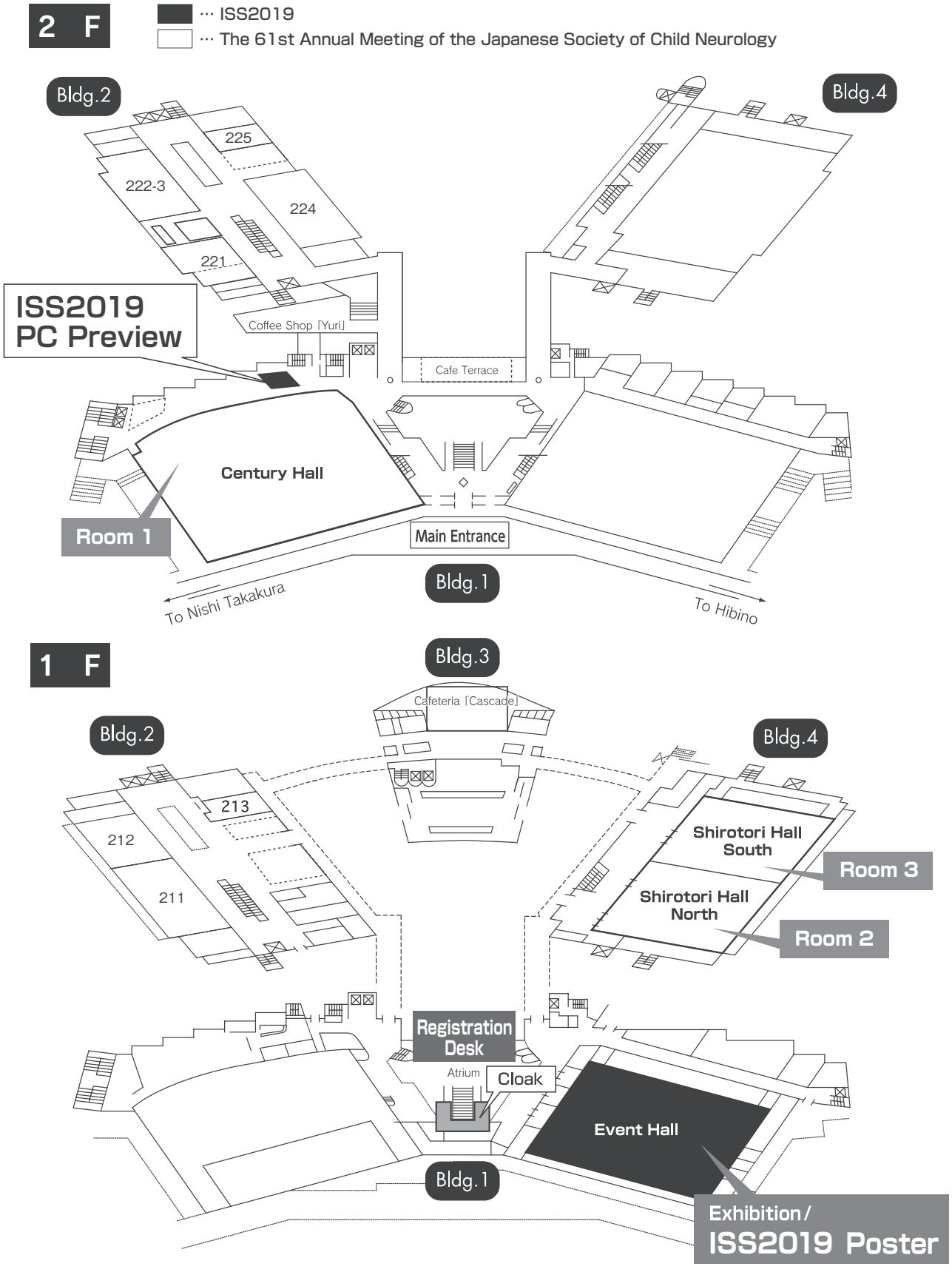

＊Room1-9 are for the 61st Annual Meeting of the Japanese Society of Child Neurology

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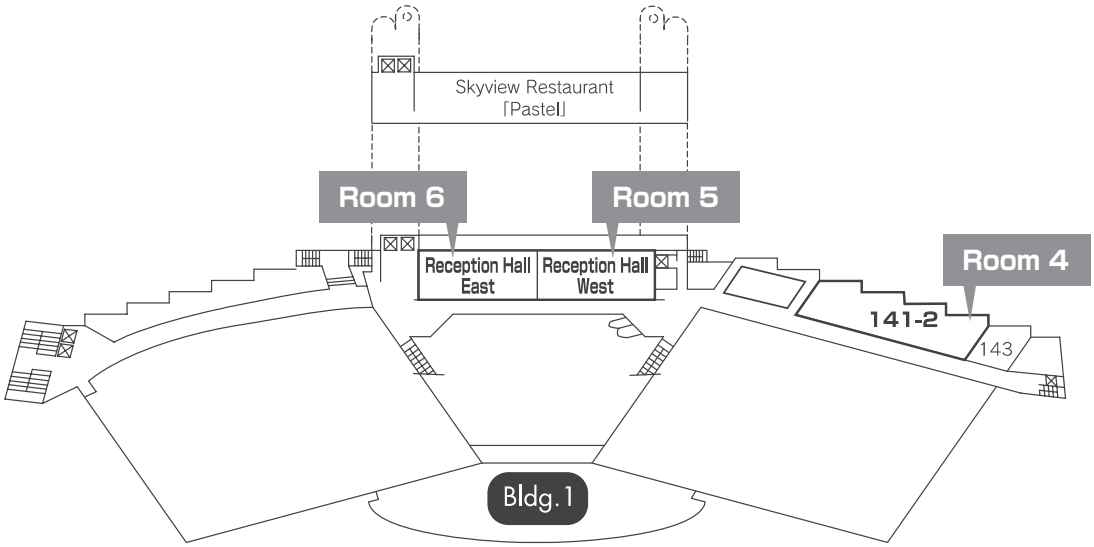
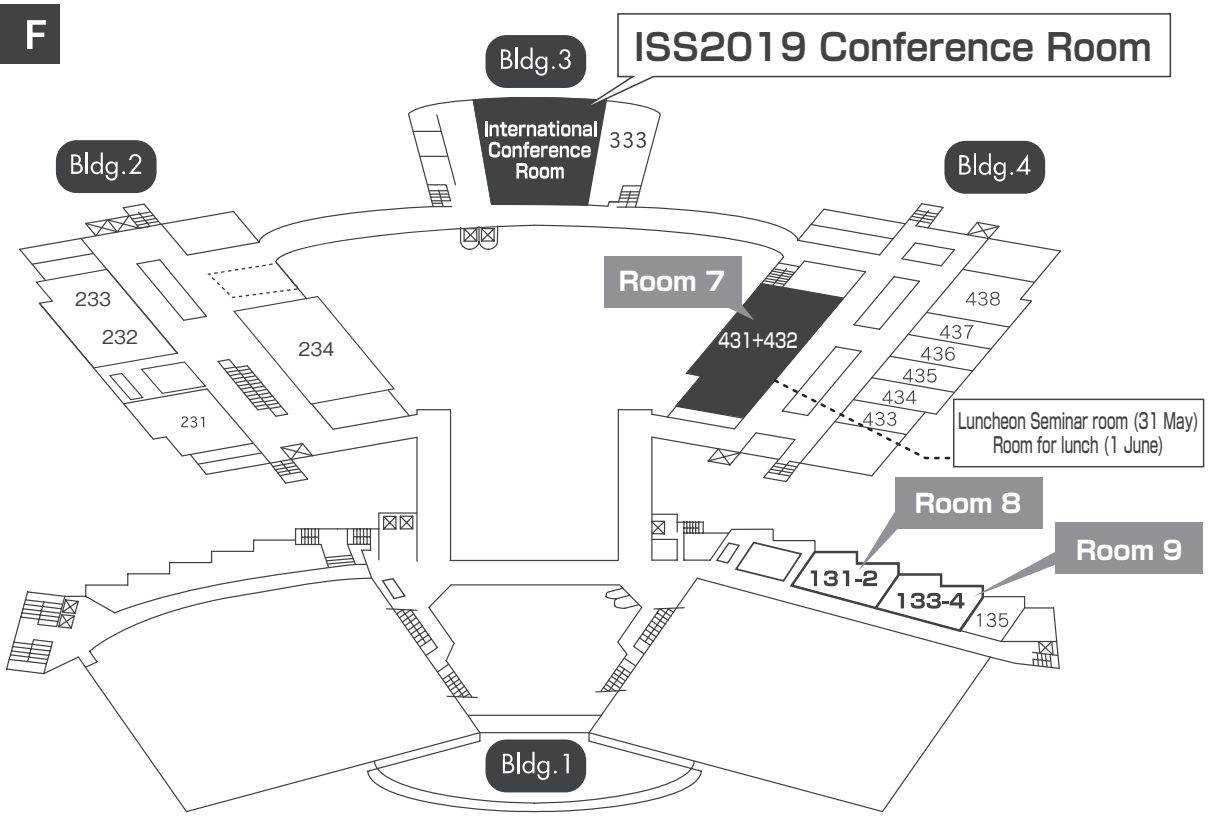

Skyview Restaurant
「Pastel」
Room 6
Room 5
Room 4
Reception Hall East
Reception Hall West
141-2
143
Bldg.1

3 F


ISS2019 Conference Room
Bldg.3
International Conference Room
333
Bldg.2
Bldg.4
Room 7
431+432
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Luncheon Seminar room (31 May)
Room for lunch (1 June)
Room 8
Room 9
131-2
133-4
135
Bldg.1

OVERVIEW of DAILY PROGRAM

Day1, Day2:At International Conference Room, 3F Bldg.3, Nagoya Congress Center
Day3:At Century Hall 2F Bldg.1, Nagoya Congress Center

Time	Day 1 31 May (Fri.)	Day 2 1 June (Sat.)	Day 3 2 June (Sun.)	Time
7:30	**Registration Desk open**	**Registration Desk open**		7:30
9:00	9:30 - 10:10 **Keynote lecture 1** Hiroyuki Kidokoro	9:00 - 9:45 **Keynote lecture 3** Geraldine B. Boylan		9:00
10:00	10:10 - 10:55 **Keynote lecture 2** Gentaro Taga	9:45 - 10:45 **Keynote lecture 4** Sampsa Vanhatalo	**Extra Session** 9:50 - 12:20 **JSCN joint symposium** **"Advance in neonatal neurology"** Sampsa Vanhatalo Geraldine B. Boylan Ronit Pressler Ritsuko K. Pooh	10:00
11:00	10:55 - 12:10 **Basic Neuroscience** Heiko J. Luhmann Kimiko Deguchi Mi-Sun Yum	10:45 - 11:05 **Abstract 2** 11:05 - 12:20 **Clinical aspects** Courtney Wusthoff Tetsuo Kubota Rhea Salonga Quimpo Derrick Wei-Shih Chan		11:00
12:00	12:25 - 13:15 **Luncheon Seminar (Room 7)** Sponsored by Eisai Co., Ltd.	12:20 - 13:30 **Lunch at Room 7**		12:00
13:00	13:30 - 14:40 **Neuroimaging** David Edwards Tetsu Niwa Katsumi Hayakawa	13:30 - 15:30 **Treatment 1** Ronit Pressler Akihito Takeuchi Jun Shibasaki Suzanne Davis Dilek Yalnizoglu Sangita Dharshini Terumalay		13:00
14:00	14:40 - 15:10 **Abstract 1**			14:00
15:00	15:10 - 16:25 **Genetics** Katherine Howell Atsushi Ishii Cheuk-Wing Fung	15:30 - 16:45 **Treatment 2** Alistair Jan Gunn Masahiro Tsuji Yoshiaki Sato Yi-Fang Tu		15:00
16:00				16:00
17:00	17:00 - 18:00 **Poster Session (Event Hall)**			17:00
18:00				18:00
19:00		19:00 - 21:00 **Childneuro 2019 in Nagoya** **Grand Social Party** **(Port of Nagoya Public**		19:00
20:00				20:00

PROGRAM

The 20th Annual Meeting of Infantile Seizure Society

PROGRAM - ORAL PRESENTATIONS

DAY1, FRIDAY, MAY 31

At International Conference Room, 3F Bldg.3, Nagoya Congress Center

Keynote lecture 1
Chairperson: Akihisa Okumura (Japan)

9:30-10:10 **L-01**

THE PATHOPHYSIOLOGY OF PRETERM BRAIN INJURIES: FROM PVL TO THE ENCEPHALOPATHY OF PREMATURITY

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

Keynote lecture 2
Chairperson: Hideo Yamanouchi (Japan)

10:10-10:55 **L-02**

FNIRS-EEG MEASUREMENT OF THE CORTEX IN SLEEPING INFANTS

Gentaro TAGA
Graduate School of Education, The University of Tokyo, Japan

Basic Neuroscience
Chairpersons: Hiroshi Sakuma (Japan), Heiko J. Luhmann (Germany)

10:55-11:35 **L-03**

HOW ELECTRICAL ACTIVITY SHAPES THE DEVELOPING BRAIN: OF NEONATAL MICE AND PRETERM HUMAN BABIES

Heiko J. LUHMANN
Institute of Physiology; University Medical Center Mainz, Germany

11:35-11:50 **L-04**

NEW ASPECTS OF EXTREMELY PRETERM INFANTS WITH BRAIN INJURY

Kimiko DEGUCHI
Deguchi Pediatric Clinic, Japan

11:50-12:05 **L-05**

A NEW ANIMAL MODEL OF INFANTILE SPASMS WITH MALFORMATION OF CORTICAL DEVELOPMENT

Mi-sun YUM
Asan Medical Center, University of Ulsan College of Medicine, Korea

Luncheon Seminar (Room7 431+342, Bldg.4, 3F, sponsored by Eisai Co., Ltd.)
Reconsideration of Epileptogenesis - From the viewpoint of E/I balance -
Chairperson: Akihisa Okumura (Japan)

12:25-12:50 **L-06**

GABAERGIC FAILURE IN EPILEPTOGENESIS -DRAVET SYNDROME AND MORE-

Norimichi HIGURASHI
Department of Pediatrics, Jikei University School of Medicine, Japan
Central Research Institute for the Molecular Pathomechanisms of Epilepsy, Fukuoka University, Japan

12:50-13:15 **L-07**

PATHOPHYSIOLOGICAL CHARACTERISTICS ASSOCIATED WITH EPILEPTOGENESIS: IMAGING OF HUMAN BRAIN SLICES

Akiyoshi KAKITA
Department of Pathology, Brain Research Institute, Niigata Univerity, Japan

Neuroimaging
Chairpersons: Jun Natsume (Japan), David Edwards (UK)

13:30-14:10 **L-08**

NETWORKS, STRUCTURE AND CONNECTIVITY IN THE DEVELOPING BRAIN

David EDWARDS
Centre for the Developing Brain, King's College London, UK

14:10-14:25 **L-09**

USEFULNESS OF MRI REGARDING NEONATAL SEIZURE

Tetsu NIWA
Tokai University School of Medicine, Japan

14:25-14:40 **L-10**

USEFULNESS OF MRI IN PERINATAL BRAIN INJURIES

Katsumi HAYAKAWA
Department of Diagnositc Radiology, Kyoto Red Cross Daiichi Hospital, Japan

Abstract 1
Chairperson: Tetsuo Kubota (Japan)

14:40-14:50 **O-1**

TRANSCRANIAL DOPPLER EXAMINATION FOR NEONATES RECEIVING THERAPEUTIC HYPOTHERMIA AND THE SEVERITY OF MRI BRAIN INJURY

Ming-chou CHIANG
Division of Neonatology, Department of Pediatrics, Chang Gung Memorial Hospital, Taiwan
Chang Gung University College of Medicine, Taoyuan, Taiwan
Study Group of Intensive and Integrated Care for Pediatric Central Nervous System (iCNS Group)

14:50-15:00 **O-2**

CONTINUOUS ELECTROENCEPHALOGRAPHIC MONITORING IN THE CRITICAL ILLNESS NEWBORN WITH HIGH RISK OF ENCEPHALOPATHY

Jainn-jim LIN
Division of Pediatric Neurology, Department of Pediatrics, Chang Gung Childrens Hospital, Taoyuan, Taiwan
Division of Pediatric Critical Care Medicine and Pediatric Neurocritical Care Center, Department of Pediatrics, Chang Gung Childrens Hospital, Taoyuan, Taiwan
Study Group of Intensive and Integrated Care for Pediatric Central Nervous System (iCNS Group)

15:00-15:10 **O-3**

PREVALENCE OF INTERICTAL SCALP EEG HIGH FREQUENCY OSCILLATIONS IN PEDIATRIC EPILEPSY MONITORING UNIT

Hiroki NARIAI
Pediatric Neurology, UCLA Mattel Children's Hospital, Los Angeles, CA, USA

Genetics
Chairpersons: Atsushi Ishii (Japan), Katherine B. Howell (Australia)

15:10-15:40 **L-11**

NEONATAL SEIZURES AND SODIUM CHANNELOPATHIES

Katherine B. HOWELL
Royal Children's Hospital Melbourne, Australia

15:40-16:10 **L-12**

GENETIC ETIOLOGY OF NEONATAL EPILEPSIES BY CAUSES OTHER THAN ABNORMALITIES OF SODIUM ION CHANNELS

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

16:10-16:25 **L-13**

GENE PANEL ANALYSIS IN NEONATAL / INFANTILE EPILEPTIC ENCEPHALOPATHY: PERSPECTIVE FROM A PAEDIATRIC NEUROLOGIST

Cheuk-Wing FUNG

Division of Neurology, Department of Paediatrics and Adolescent Medicine, Hong Kong Children's Hospital, Hong Kong

DAY2, SATURDAY, JUNE 1

At International Conference Room, 3F Bldg.3, Nagoya Congress Center

Keynote lecture 3
Chairperson: Akihisa Okumura (Japan)

9:00-9:45 **L-14**

NEUROPHYSIOLOGICAL ASPECTS OF NEONATAL SEIZURES

Geraldine B. BOYLAN
INFANT Centre, University College Cork, Ireland

Keynote lecture 4
Chairperson: Akira Oka (Japan)

9:45-10:45 **L-15**

BASIC RESEARCH ON PHYSIOLOGY OF FETAL-NEONATAL BRAIN

Sampsa VANHATALO
Children's Hospital, Helsinki University Hospital, Finland

Abstract 2
Chairperson: Shin-ichiro Hamano (Japan)

10:45-10:55 **O-4**

INCREMENT OF GABA NEUROTRANSMISSION IN KCNQ2 GENE MUTATION MODEL OF NEONATAL EPILEPSY

Taku UCHIDA
Department of Neuroscience, Section of Integrative Physiology, Faculty of Medicine, University of Miyazaki, Japan
Central Research Institute for the Pathomechanisms of Epilepsy, Fukuoka University, Japan

10:55-11:05 **O-5**

INFANTILE EPILEPTIC ENCEPHALOPATHIES: EVALUATING IN THREE CASES

Ozlem YAYICI KOKEN
SBU, Dr Sami Ulus Research and Training Hospital, Ankara, Turkey

Clinical aspects
Chairpersons: Kenjiro Kikuchi (Japan), Courtney J. Wusthoff (USA)

11:05-11:35 **L-16**

CLINICAL MANIFESTATIONS OF NEONATAL SEIZURES

Courtney J. WUSTHOFF
Stanford University, USA

11:35-11:50 **L-17**

APPLICATION OF NEW NEONATAL SEIZURE CLASSIFICATION

Tetsuo KUBOTA
Department of Pediatrics, Anjo Kosei Hospital, Japan

11:50-12:05 **L-18**

NEONATAL EPILEPSIES: A PRACTICAL APPROACH

Rhea Angela SALONGA-QUIMPO
Section of Pediatric Neurology, Department of Neurosciences, University of the Philippines-Philippine General Hospital, Phillipines

12:05-12:20 **L-19**

INBORN ERRORS OF METABOLISM IN NEONATAL SEIZURES

Derrick Wei-shih CHAN
KK Women's and Children's Hospital, Singapore

Treatment 1
Chairpersons: Masahiro Hayakawa (Japan), Ronit Pressler (UK)

13:30-14:00 **L-20**

TREATMENT AND EEG MONITORING FOR NEONATAL SEIZURES

Ronit PRESSLER
Great Ormond Street Hospital for Children, UCL Great Ormond Street Institute of Child Health, UK

14:00-14:15 **L-21**

ANTIEPILEPTIC TREATMENT FOR NEONATAL SEIZURES

Akihito TAKEUCHI
Division of Neonatology and Neuropediatrics, National Hospital Organization Okayama Medical Center, Japan

14:15-14:30 **L-22**

HYPOTHERMIA FOR NEONATAL SEIZURES

Jun SHIBASAKI
Department of Neonatology, Kanagawa Children's Medical Center, Kanagawa, Japan

14:30-14:45 **L-23**

THE NEOLEV2 TRIAL. WHAT HAVE WE LEARNED ABOUT THE MANAGEMENT OF NEONATAL SEIZURES?

Suzanne L. DAVIS
Starship Children's Hospital, New Zealand

14:45-15:00 **L-24**

APPROACH TO NEONATAL SEIZURES AT A TERTIARY HOSPITAL IN TURKEY

Dilek YALNIZOGLU
Hacettepe University Faculty of Medicine, Turkey

15:00-15:15 **L-25**

DIAGNOSIS AND TREATMENT FOR NEONATAL SEIZURES IN MALAYSIA

Sangita D. TERUMALAY
Department of Pediatrics, Pediatric Institute, Hospital Kuala Lumpur Malaysia, Malaysia

Treatment 2
Chairpersons: Hideaki Shiraishi (Japan), Alistair Jan Gunn (New Zealand)

15:30-16:00 **L-26**

HOW TO PROTECT THE NEONATAL BRAIN

Alistair J. GUNN
University of Auckland, New Zealand

16:00-16:15 **L-27**

UMBILICAL CORD BLOOD STEM CELL THERAPY FOR NEONATAL ENCEPHALOPATHY

Masahiro TSUJI
Kyoto Women's University, Japan

16:15-16:30 **L-28**

DEVELOPMENT A NOVEL REGENERATIVE TREATMENT FOR PERINATAL BRAIN INJURY WITH MUSE CELLS

Yoshiaki SATO
Nagoya University Hospital, Japan

16:30-16:45 **L-29**

NEUROLOGICAL OUTCOMES IN INFANTS WITH NEONATAL SEIZURES RELATED TO HYPOXIC-ISCHEMIC ENCEPHALOPATHY

Yi-Fang TU
Department of Pediatrics, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan

EXTRA SESSION, SUNDAY, JUNE 2

At Century Hall 2F Bldg.1, Nagoya Congress Center

JSCN joint symposium "Advance in neonatal neurology"
Chairpersons: Akihisa Okumura (Japan), Sampsa Vanhatalo (Finland)

9:50-12:20

1) NEONATAL EEG

Sampsa VANHATALO
BABA center, Children's Hospital, University of Helsinki, Finland

2) A NEONATAL SEIZURE DETECTION ALGORITHM

Geraldine B. BOYLAN
INFANT Research Centre, Ireland

3) NEW NEONATAL SEIZURE CLASSIFICATION

Ronit PRESSLER
Great Ormond Street Hospital for Children, UK

4) NEUROIMAGING OF DEVELOPING BRAIN BEFORE BIRTH

Ritsuko K. POOH
CRIFM Clinical Research Institute of Fetal Medicine PMC, Japan

*The participants of ISS2019 can join this session.

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PROGRAM - POSTER SESSION

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ELECTROPHYSIOLOGICAL PROPERTIES OF EXCITATORY OR INHIBITORY NEURONS DERIVED FROM INDUCED PLURIPOTENT STEM CELLS (IPSC) IN ANGELMAN SYNDROME

Kiyoshi EGAWA Department of Pediatrics, Hokkaido University Graduate school of Medicine, Japan

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ASSOCIATION BETWEEN BRUSH OCCURENCE ON ELECTROENCEPHALOGRAM AND NEURODEVELOPMENTAL OUTCOME IN PREMATURE INFANTS

Takashi MAEDA Department of Pediatrics Cardiology and Neonatology, Ogaki Municipal Hospital, Japan

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CLINICAL FEATURES AND ELECTROCLINICAL EVOLUTION OF 22 PATIENTS WITH EPILEPTIC SPASMS WITHOUT HYPSARRHYTHMIA

Reiko KOICHIHARA Neurology, Saitama Children's Medical Center, Japan

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EEG-FMRI ANALYSIS OF HYPSARRHYTHMIA IN WEST SYNDROME OF UNKNOWN ETIOLOGY

Yu OKAI Department of Pediatrics, Nagoya University Graduate School of Medicine, Nagoya, Japan
Brain and Mind Research Center, Nagoya University, Nagoya, Japan

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CLINICO-ELECTROENCEPHALOGRAPHIC STUDY OF REPETITIVE SLEEP STARTS IN CHILDREN

Yuki MAKI Department of Pediatrics, Nagoya University Graduate School of Medicine, Japan

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ASSOCIATION OF GRAY MATTER VOLUME IN PRETERM INFANTS WITH NEURODEVELOPMENTAL OUTCOMES

Hiroyuki KIDOKORO Nagoya University, Japan

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GLYCINE MEASUREMENT USING SHORT AND LONG ECHO TIME PROTON MAGNETIC RESONANCE SPECTROSCOPY IN A NEONATE WITH NONKETOTIC HYPERGLYCINEMIA

Ayana HIROSE Kanagawa Children's Medical Center, Japan

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123I-IOMAZENIL SPECT FINDINGS IN CRYPTOGENIC WEST SYNDROME

Satoru IKEMOTO Department for Child Health and Human Development, Saitama Childrens Medial Center, Japan
Division of Neurology, Saitama Childrens Medical Center, Japan

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DOES HYPSARRYTHMIA AFFECT RCBF IN THE PATIENTS WITH EPILEPTIC SPASMS?

Yuko HIRATA Division of Neurology, Saitama Children's Medical Center, Japan

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DE NOVO PHACTR1 MUTATIONS IN WEST SYNDROME AND THEIR PATHOPHYSIOLOGICAL EFFECTS

Nanako HAMADA Department of Molecular Neurobiology, Institute for Developmental Research, Japan

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GENETIC HETEROGENEITY IN MYOCLONIC ASTATIC EPILEPSY OR DOOSE SYNDROME

Nodoka HINOKUMA Department of Pediatrics, Showa University School of Medicine, Japan

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DIFFERENT PHENOTYPES IN THREE PATIENTS WITH *SCN2A* VARIANT

Shinichiro MORICHI Department of Pediatrics, Tokyo Medical University, Japan

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DISSECTING THE PHENOTYPIC AND GENETIC SPECTRUM OF EARLY CHILDHOOD-ONSET GENERALIZED EPILEPSIES

Soo Yeon KIM Seoul National University Children's Hospital, Korea

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THE PREDICTIVE FACTORS FOR LATER DEVELOPMENT OF EPILEPSY IN INFANTS WITH VERY LOW BIRTH WEIGHT

Toshimichi FUKAO Department of Pediatrics, Faculty of Medicine, University of Yamanashi, Japan
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RASMUSSEN SYNDROME: ASSESSMENT OF CLINICAL FEATURES IN PATIENTS WITH DIFFERENT INTELLECTUAL LEVELS

Taira TOKI Department of Child Neurology National Center Hospital, National Center of Neurology and Psychiatry, Japan

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Shohei KUSABIRAKI Department of Pediatrics, Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama, Toyama, Japan

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PERAMPANEL AS EFFECTIVE ADD-ON ANTIEPILEPTIC DRUG FOR REFRACTORY EPILEPSY IN A PATIENT WITH MECP2 DUPLICATION SYNDROME

Yu Min SYU Far Eastern Memorial Hospital, Taipei, Taiwan

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Ryosuke URABE Division of Neurology, National Center for Child Health and Development, Japan

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Konomi SHIMODA The Department of Pediatrics, University of Tokyo, Japan

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Taikan OBOSHI Osaka Prefectural Hospital Organization Osaka Women's and Children's Hospital, Japan

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Kaori SASSA Department of Pediatrics, Saitama Medical University Hospital, Japan
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Ayana SUNAGA Department of Pediatrics, Osaka City University Graduate School of Medicine, Japan

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Takuya HAYASHIDA Department of Pediatrics, Nagasaki University Hospital, Japan

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

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Takahiro ABIKO Department of Pediatrics, Faculty of Medicine, Yamagata University, Japan

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Meltem UZUN Private Dr.Meltem Uzun Pediatric Neurology Clinics, Turkey

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

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A CASE OF TYROSINE HYDROXYLASE (TH) DEFICIENCY: CLINICAL COURSE WITH ORAL TREATMENT

Kozue KUWABARA Ehime Prefectural Central Hospital, Japan

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AN INFANT WITH DIETARY VITAMIN B12 DEFICIENCY DUE TO MATERNAL ANTIBODIES PRESENTING WITH WEST SYNDROME

Pin Fee CHONG Department of Pediatric Neurology, Fukuoka Children's Hospital, Japan

P-30

PERAMPANEL AND KETOGENIC DIET IN WEST SYNDROME DUE TO NEONATAL NONKETOTIC HYPERGLYCINEMIA: A CASE REPORT

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Division of Pediatrics, Tokyo Medical University, Japan

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A CASE OF FATAL LEGIONELLA PNEUMONIA DURING ACTH THERAPY FOR WEST SYNDROME

Hironao SHIRAI Kitasato University Hospital Department of pediatrics, Japan

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A CHILD WITH MOVEMENT DISORDER MIMICKING SEIZURE IN GNAO1 RELATED ENCEPHALOPATHY

Leechin WONG Cathay general hospital, Taiwan

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DYT1 EARLY-ONSET ISOLATED DYSTONIA

Feng-chin LEE Tri-Service general Hospital, Taiwan

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NEONATAL ABNORMAL MOVEMENTS FOLLOWED BY INFANTILE SPASMS CAUSED BY THE KCNQ2 R198Q MUTATION

Sho NARAHARA Anjo Kosei Hospital, Department of Pediatrics, Japan

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A CASE OF EARLY INFANTILE-ONSET LEIGH SYNDROME WITH A M.9185T>C IN THE MTATP6 GENE MUTATION COMPLICATED WITH INFANTILE SPASMS

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A PATIENT WITH LENNOX-GASTAUT SYNDROME CAUSED BY PACS2 GENE MUTATION

Rie MIYATA Tokyo-Kita Medical Center, Japan

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Syuan-yu HONG Division of Pediatrics Neurology, Taiwan

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Kazuhiko HASHIMOTO Department of Pediatrics, Nagasaki University Hospital, Japan

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A CASE OF DEVELOPMENTAL AND EPILEPTIC ENCEPHALOPATHY CAUSED BY A NOVEL SCN2A GENE VARIAN

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A CASE OF SCN8A-ASSOCIATED EPILEPTIC ENCEPHALOPATHY CAUSED BY A NOVEL HETEROZYGOUS MUTATION: WHERE IS THE ORIGIN OF REFRACTORY STARTLE REFLEX AND MYOCLONUS?

Nahoko KUEDA Division of Neurology, National Center for Child Health and Development, Japan

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CORPUS CALLOSOTOMY FOR EPILEPTIC SPASMS OR TONIC SEIZURES IN PATIENTS WITH TUBEROS SCLEROSIS COMPLEX

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Division of Child Neurology, Department of Brain and Neurosciences, Faculty of Medicine, Tottori University, Yonago, Japan
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EARLY DIFFERENTIATION OF ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION FROM FEBRILE STATUS EPILEPTICUS USING EEG ANALYSIS

Shota AKIYAMA Department of Pathological Science and Technology, School of Life Sciences, Tottori University Faculty of Medicine, Yonago, Japan

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A CASE OF INFLUENZA ASSOCIATED ENCEPHALOPATHY WITH LATE REDUCED DIFFUSION OBSERVED SURROUNDING PRE-EXISTING FOCAL CORTICAL LESION

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ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION: COMPARISON BETWEEN INFLUENZA AND HHV6/7

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ACUTE ENCEPHALOPATHY WITH NONCONVULSIVE STATUS EPILEPTICUS IN ROTAVIRUS GASTROENTERITIS

Ko HIRATA Soka Municipal Hospital, Japan

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ASSOCIATION OF RARE NONSYNONYMOUS VARIANTS OF *SCN1A* WITH ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION

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INFLUENZA-ASSOCIATED CNS COMPLICATIONS IN FEBRILE CHILDREN: ELEVATED ALT MAY BE AN EARLY HINT OF ACUTE NECROTIZING ENCEPHALOPATHY

Yu WENHAO Department of Pediatrics, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan

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THREE CASES PRESENTING WITH TRANSIENT EDEMATOUS BRAIN LESIONS AFTER FEBRILE STATUS EPILEPTICUS

Kazuna YAMAMOTO Teikyo University, Japan

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Cheng Yen KUO Division of Pediatric Neurology, Chang Gung Children Hospital and Chang Gung Memorial Hospital, Taoyuan, Taiwan

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TREATMENT AND SHORT-TERM PROGNOSIS OF CONVULSIVE REFRACTORY STATUS EPILEPTICUS IN CHILDREN

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Division of Neurology, Saitama Children's Medical Center, Japan

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ENTEROVIRUS D68 NEUTRALIZING ANTIBODY IN CULTURE-NEGATIVE ACUTE FLACCID MYELITIS

Li-wen CHEN Department of Pediatrics, National Cheng Kung University Hospital, Taiwan

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POST VACCINATION CONVULSION RARE IN BANGLADESH-A COMPREHENSIVE STUDY

Mir ANWAR Richmond Chest Hospital, South Africa

ABSTRACTS

L-01

THE PATHOPHYSIOLOGY OF PRETERM BRAIN INJURIES: FROM PVL TO THE ENCEPHALOPATHY OF PREMATURITY

Hiroyuki KIDOKORO

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

Periventricular leukomalacia (PVL) is the classical form of brain injury in preterm infants. However, several issues regarding PVL remain unresolved. For example, the precise mechanisms underlying PVL are not yet fully understood and it is not possible to identify precisely the time of injury in these patients. EEG findings play an important role in understanding the pathological features of PVL, and the detection of acute- and chronic-stage EEG abnormalities allow researchers to assess PVL-related issues.

Recent advances in the perinatal and neonatal care of preterm infants have reduced the incidence of severe brain injuries such as PVL, periventricular hemorrhagic infarction. However, the rates of cognitive and behavioral deficits remain high and stable, as approximately 50% of extremely premature infants exhibit disabilities in these domains. Recent MRI and EEG studies have revealed structural and functional alterations in preterm brains without apparent brain injury. This suggests that brain injury cannot fully explain neurodevelopmental impairments and, therefore, alterations in brain development must play a role.

Subplate neurons have a transient existence during fetal life but play important roles in the network development, and also contribute to the development of the cortical inhibitory system. Subplate neuronal activities are likely to be reflected as a delta brush, which is a characteristic component of background activity seen on preterm EEG findings. Alterations in the activities of these neurons may contribute to the underlying mechanisms of the cognitive and behavioral deficits that are evident in extremely premature infants. I will present evidence regarding this topic.

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2000–2001 Clinical Fellow, Department of Pediatrics, Anjo Kosei Hospital
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Academic Positions
2010-2012: Postdoctoral Research Associate, Department of Pediatrics, Washington University in St. Louis
2014–present: Assistant Professor, Department of Pediatrics, Nagoya University Graduate School of Medicine, Nagoya, Japan

Licensure/Certification:
- Certified National Board for the Medical Doctor in Japan, May 1998
- Certified Pediatrician of the Japan Pediatric Society, May 2005
- Certified The Japanese Board of Child Neurology, November 2007
- Certified Board of Japan Epilepsy Society, October 2017

Specialized Field:
Pediatrics, Child Neurology, Neonatology, Neonatal Neurology, Epileptology

Awards and Honors:
2016 The 58th annual meeting of the Japanese society of child neurology: Best Oral Award

Selective publications:

FNIRS-EEG MEASUREMENT OF THE CORTEX IN SLEEPING INFANTS

L-02

Gentaro TAGA

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Sleep states reflect spontaneous activity of the brain. The gold standard for classification of sleep states is to use the electroencephalogram (EEG) and electrooculogram (EOG). On the other hand, the functional near infrared spectroscopy (fNIRS) can measure cortical tissue oxygenation related to the neural activity due to neurovascular coupling. Especially, fNIRS has been used to young infants to elucidate the spontaneous cortical activity during sleep (Taga et al. 2000), stimulus induced activity during waking and sleeping (Taga et al. 2003, 2018), functional network (Homae et al. 2010), and hemoglobin phase of oxygenation and deoxygenation (hPod) (Watanabe et al. 2017). Here I will show fNIRS provides distinct properties of spontaneous changes in cortical oxygenation depending on sleep states of infants. We measured the wide regions of the cortex of 2- and 3-month-old infants by using 94 channel fNIRS while they were naturally sleeping in the laboratory in the daytime. Sleep states were classified into active sleep (AS), quiet sleep (QS), AS/QS and wake by using EEG, EOG and video recordings. Instantaneous phases of oxy- and deoxy-hemoglobin signals were extracted from Hilbert transformation of bandpass-filtered time-series data and phase synchronization index (PSI) among 94 channels was obtained (Taga et al. 2011). Comparisons of time-averaged PSIs between the AS and QS revealed that the phase synchronization among the global cortical regions is enhanced in AS and diminished in QS. Thus, fNIRS can provide new information on the cortical development in relation to the control of sleep states in young infants.

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Gentaro Taga is a professor at Graduate School of Education, The University of Tokyo.

He received the Ph. D. degree in pharmaceutical sciences (biophysics) from University of Tokyo in 1994. He was a JSPS postdoctoral fellow at Yukawa Institute for Theoretical Physics, Kyoto University and Neuro-Muscular Research Center, Boston University in 1994. He joined the complex system research group as an assistant professor at Department of Pure and Applied sciences, University of Tokyo in 1995. In 2000, he established Developmental Brain Science Laboratory at Graduate School of Education, University of Tokyo. He was a visiting scholar at California Institute of Technology, University Hospital Zurich, and Konrad Lorenz Institute for Evolution and Cognition Research.

He was awarded 1st Japan Society for the Promotion of Sciences Prize in 2004.

L-03

HOW ELECTRICAL ACTIVITY SHAPES THE DEVELOPING BRAIN: OF NEONATAL MICE AND PRETERM HUMAN BABIES

Heiko J. LUHMANN

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At very early developmental stages, a large number of brain regions show a surprisingly rich repertoire of spontaneous activity. In sensory systems, this activity often arises from spontaneous activity patterns in the sensory periphery, like the retina or the cochlea. In the somatosensory system, different motor areas may function as pattern generators and elicit spontaneous movements, which subsequently activate the somatosensory system. Spontaneous activity in cortical areas plays an important role in the control of programmed cell death and the formation of local networks and cortical columns. The subplate, a transient layer located between the cortical plate / layer 6 and the white matter, is essential to transmit and amplify spontaneous activity patterns from the thalamus to the developing cortex. Modifications in these early spontaneous activity patterns, induced for example by pre- or neonatal drug exposure, hypoxia-ischemia or inflammation, may have an impact on cortical development with long-term consequences.

This presentation will link clinical data obtained in preterm/neonatal human babies to experimental data obtained in animal models with the aim to contribute to a better understanding of the physiological and pathophysiological aspects of early cortical development.

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Academic education with degrees

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1977 - 1983	Biology (Diploma), University of Bremen

Scientific degrees

1994	Habilitation in Physiology, Medical Faculty Univ. of Cologne
1987	Dr. rer. nat.: Biology, University of Bremen

Professional career

since 2016	Deputy speaker of the CRC 1080 "Molecular and cellular mechanisms of neural homoesostasis"
2010 - 2015	Speaker and coordinator of the Swiss-German Research Unit "Barrel Cortex Function" (DFG-FOR 1341)
2004 - 2013	Speaker and coordinator of the Neuroscience Graduate Program "Development-dependent and disease-induced modifications in the nervous system" (DFG GRK 1044/1), Johannes Gutenberg-University Mainz
since 2002	C4/W3 Professor of Physiology at the Medical Center of Johannes Gutenberg-University, Mainz
1997 - 2002	Speaker and coordinator of the Neuroscience Graduate Program "Pathological processes in the nervous system: from gene to behavior" (DFG GRK 320), University of Düsseldorf
1995 - 2002	C3-Professor of Physiology at the University of Düsseldorf
1994 - 1995	Assistant professor at the Institute of Physiology, Charité, Department of Neurophysiology, Humboldt-University Berlin
1990 - 1994	Research assistant at the Institute of Neurophysiology at the University of Cologne (Uwe Heinemann, M.D.)
1987 - 1990	Postdoctoral fellow of the Deutsche Forschungsgemeinschaft at the Department of Neurology at Stanford University School of Medicine (David Prince, M.D.)
1985 - 1987	Doctoral student, supervisor: Wolf Singer (M.D.), MPI Brain Research, Frankfurt

Reseach interests

Neurophysiology, developmental neurobiology

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1992	Bennigsen-Foerder Award received from Ministry of Innovation, Science and Research of the State of North Rhine-Westphalia, Germany
1992 – 1990	DFG Postdoc Fellowship, Department of Neurology and Neurological Sciences, Stanford University, USA

Other professional activities

since 2015	Member of the DFG Grants Committee for Collaborative Research Centres
since 2013	Editor in Chief "Neuroforum" and "e-Neuroforum", the Journal of the German Neuro-science Society (Neurowissenschaftliche Gesellschaft)
2011-2016	Section Editor "Neuroscience" - The journal of The International Brain Research Organization (IBRO)
2013/14	President of German Physiological Society (Deutsche Physiologische Gesellschaft)
2012-2014	Committee member of Network European Neuroscience Schools (NENS) of FENS
2009-2014	Member of Neuroscience review panel (Fachkollegium) at DFG

Member of external review board at GIGA-Neurosciences (University of Liège, Belgium), INSERM Strasbourg (France) and Neurocentre Magendie / INSERM u862 (Bordeaux, France).

NEW ASPECTS OF EXTREMELY PRETERM INFANTS WITH BRAIN INJURY

L-04

Kimiko DEGUCHI

Deguchi Pediatric Clinic, Japan

In the last decade, cognitive impairment with neurodevelopmental disorders has been recognized as a more common neurological outcome of extremely preterm infants (EPIs, born before 28 gestational weeks (GWs)) with brain injury than cerebral palsy. Previous studies of brain injuries in EPIs have mainly delineated pathological alterations in oligodendrocytes and problems in neuronal network. We recently reported that a large number of ectopic neurons are present in the subcortical white matter in EPIs with brain injury and hypothesized that altered neuronal migration may be associated with cognitive impairment in later life. To confirm whether preterm brain injury affects neuronal migration, we generated a mouse model of EPIs by occluding the maternal uterine arteries to produce brain damage in mouse embryos. The mice showed that delayed neuronal migration and ectopic neurons in the white matter, which resulted in altered synaptic formations and abnormal neuronal network, probably leading to cognitive dysfunction and behavior problems in these mice. Postnatal pharmacological activation of the affected medial prefrontal cortices improved working memory deficits, indicating that decreased neuronal activity caused the cognitive deficits, which can be modified at last in mice. All these findings nicely mimic human EPIs with brain injury and these mice may serve as a plat form to study brain injury in EPIs. We emphasize that the key aspect of cognitive impairment in EPIs with brain injury is the altered neuronal migration and network, which probably contribute to the subsequent development of cognitive impairment with neurodevelopmental disorders.

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Residency	National Nagasaki Center Hospital	1988-1990	
Clinical Fellow	Kanagawa Children's Medical Center, Japan	1992-1993	Pediatric Neurology
Research Fellow	National Institute of Neuroscience, National Center of Neurology and Psychiatry (NCNP)	1993-1997	Pediatric Neuropathology
Postdoctoral Fellow	Baylor College of Medicine	1997-2007	Pediatric Neuropathology Pediatric Neurology Molecular & Human Genetics

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5/06 –present Director, Deguchi Pediatric Clinic, Nagasaki, Japan
4/12- present Part time Lecturer, Department of Anatomy, Keio University School of Medicine, Tokyo, Japan
・BOARD CERTIFICATIONS:</h1>
Board Certified Pediatrics (Japan)
RESEARCH INTEREST:
Determine the disease mechanisms for human brain injury in extremely preterm infants (EPIs) using neuropathological approach and the disease mouse model.
Determine disease mechanisms and identify treatments for human EPIs with brain injury

L-05

A NEW ANIMAL MODEL OF INFANTILE SPASMS WITH MALFORMATION OF CORTICAL DEVELOPMENT

Mi-sun YUM

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Malformations of cortical development (MCD) can cause intractable epilepsies including epileptic spasms and cognitive disabilities in children. Despite the serious neurodevelopmental sequelae of epileptic spasms during infancy, the pathomechanisms involved remain unclear. To find potential biomarkers or treatment regimens that can reflect the pathogenesis of epileptic encephalopathy, we developed a new model of MCD-associated epileptic spasms by treating rats prenatally with methylazoxymethanol acetate (MAM) to induce cortical malformations and postnatally with N-methyl-d-aspartate (NMDA) to induce spasms. Using this new animal model of infantile spasms, we tried to explore the neurometabolic and microstructural changes after infantile spasms.

To produce cortical malformations to infant rats, two dosages of MAM were injected to pregnant rats at gestational day 15. In prenatally MAM-exposed rats and the controls, spasms were triggered by single or multiple doses (P12, P13, and P15) of NMDA. In prenatally MAM-exposed rats with single NMDA-provoked spasms at P15, we obtain the intracranial electroencephalography and examine the pretreatment response to ACTH or vigabatrin. Rat pups prenatally exposed to MAM exhibited a significantly greater number of spasms in response to single and multiple postnatal NMDA doses than controls. Vigabatrin treatment prior to a single NMDA dose on P15 significantly suppressed spasms in MAM group rats. The MAM group also showed significantly higher fast oscillation (25-100 Hz) power during NMDA-induced spasms than controls. This new model of MCD-based epileptic spasms with corresponding features of human spasms will be valuable for future research of the developmental epilepsy.

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Mar. 2002 - Feb. 2006 : Residency Department of Pediatrics Asan Medical Center, Seoul, Korea

Positions Held & Faculty Appointment
Feb. 2006 – Feb. 2009. : Fellow Division of Pediatric Neurology, Department of Pediatrics, Asan Medical Center, Seoul, Korea
Mar.2009-Apr.2010 : Visiting Scientist Department of Neurology at the Albert Einstein College of Medicine
May 2010-present : Division of Pediatric Neurology, Department of Pediatrics, Asan Medical Center, Seoul, Korea
Current position, associate professor

Licensure and Certification
Licenced to Practice Medicine in Korea, 2001
Korean Board of Pediatrics, 2006
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GABAERGIC FAILURE IN EPILEPTOGENESIS -DRAVET SYNDROME AND MORE-

L-06

Norimichi HIGURASHI[1,2]

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Alterations of gamma-aminobutyric acid-mediated (GABAergic) functions have been identified in a wide range of brain diseases, including epilepsy and are thought to be at least partly involved in the basis of those diseases. Epilepsy has a variety of etiologies that act to induce an imbalance between excitatory and inhibitory mechanisms. It was long considered that neuronal hyperexcitability precipitating epilepsy simply resulted from increased excitation and/or reduced inhibition, with GABAergic mechanisms inducing the latter effect by specifically reducing phasic inhibition mediated via synaptic $GABA_A$ receptors. This mechanism is well represented in Dravet syndrome, a form of infantile-onset, drug-resistant epilepsy mainly caused by *SCN1A* defects. However, recent findings have indicated that GABAergic mechanisms have a more complicated role in epilepsy and do not always simply reduce neuronal inhibition. For example, an excitatory depolarizing response mediated by $GABA_A$ receptors, which is normally observed in the developing brain, has also been demonstrated in epileptic brain tissues and shown to enhance epileptic activity. In addition to phasic inhibition, alterations of tonic inhibition mediated by extrasynaptic $GABA_A$ receptors contribute to epilepsy (e.g., enhanced tonic inhibition in patients with absence seizures). Furthermore, diversity of GABAergic influences is also increasingly being recognized in Dravet syndrome. In this presentation, I will briefly review the basics of GABAergic neurotransmission and present several key examples of the role of GABAergic mechanisms in epilepsy, mainly highlighting our updated understanding of the pathophysiology of Dravet syndrome.

CURRICULUM VITAE

Dr. Higurashi graduated and obtained his MD (2001) and PhD (2013) degrees at Jikei University School of Medicine. He has spent most of his career taking care of sick children, particularly with neurological diseases. In 2009, he started research on the genetics and cellular/molecular pathomechanisms of early onset epilepsies at Fukuoka University (Prof. Shinichi Hirose) in collaboration with Keio University (Prof. Hideyuki Okano). In a groundbreaking study, he succeeded in replicating the pathology of Dravet syndrome by using patient-derived induced pluripotent stem cells in 2013. He also contributed to the current understanding of many clinical aspects of PCDH19-related epilepsy. Now, he continues basic research on pediatric epilepsies by obtaining research grants mainly from the Japan Society for the Promotion of Science and Japan Agency for Medical Research and Development. He also served as a taskforce member for ILAE and was involved in the establishment of the 2017 seizure type classification.

L-07

PATHOPHYSIOLOGICAL CHARACTERISTICS ASSOCIATED WITH EPILEPTOGENESIS: IMAGING OF HUMAN BRAIN SLICES

Akiyoshi KAKITA

Department of Pathology, Brain Research Institute, Niigata Univerity, Japan

Seizure activities often originate from a localized region of the cerebral cortex and spread across large areas of the brain. The properties of these spreading abnormal discharges may account for clinical phenotypes in epilepsy patients, although the underlying mechanisms are not well understood. We investigated epileptiform activities ex vivo using epileptogenic brain tissue surgically resected from patients with partial epilepsy caused by various symptomatic lesions. Children with hypothalamic hamartoma often have characteristic gelastic seizures. In terms of the pathophysiology of this malformation, our recent physiological and morphological study using needle biopsy specimens revealed that Ca2+ permeability in neurons through AMPA receptors was aberrantly elevated, and that the neuronal nuclei showed disappearance of ADAR2 immunoreactivity. Flavoprotein fluorescence imaging and local field potential recordings of hippocampal specimens taken from patients with mesial temporal lobe epilepsy (MTLE) revealed that the epileptiform activity was often observed in the subiculum, not in the hippocampus proper. In accordance with increasing the extracellular K+ concentration ([K+]o) in culture media for the hippocampal tissue slices, peak frequency of HFOs of patients with MTLE was significantly higher than that of the control, suggesting impairment of extracellular K+ clearance mechanisms in the subiculum. Loss of immunoreactivity for inwardly rectifying K+ channel 4.1 (Kir 4.1) in astrocytes in the subiculum was also evident. Thus, impairment of homeostatic [K+]o by glial Kir4.1 may play a pivotal role for the development of MTLE. Thus, an integrated approach by using various methodologies may be crucial for better understanding pathomechanisms of the epileptic disorders.

CURRICULUM VITAE

EDUCATION

NIIGATA UNIVERSITY POST-GRADUATE COURSE
Pathology (Neuropathology), Brain Research Institute, Niigata University, Japan
Doctor of Medical Science (Ph.D.), 1993

NIIGATA UNIVERSITY SCHOOL OF MEDICINE
Doctor of Medicine (MD), 1989

TRAINING AND RESEARCH

BRAIN RESEARCH INSTITUTE, NIIGATA UNIVERSITY, Niigata, Japan
- ***Deputy Director*** 2017-present
- ***Professor of Pathology*** 2011-present
  Department of Pathology and The Resource Branch for Brain Disease Research CBBR
- ***Associate Professor of Pathology*** 2000-2011
  Department of Pathology Neuroscience, Resource Branch for Brain Disease Research CBBR
- ***Research Assistant*** 1995-2000
  Department of Pathology
- ***Postdoctoral Fellow*** 1993-1995
  Department of Pathology

COLUMBIA UNIVERSITY 1997-1999
COLLEGE OF PHYSICIANS AND SURGEONS, New York, NY, USA
- ***Postdoctoral Fellow***
  Department of Pathology

RECENT PUBLICATIONS

1. Tainaka K, *et al.* Chemical landscape for tissue clearing based on hydrophilic reagents. **Cell Rep** 2018; 38: 428-432.
2. Ishiura H, *et al.* Intronic TTTCA and TTTTA repeat expansions in benign adult familial myoclonic epilepsy. **Nat Genet** 2018; 38: 428-432.
3. Kitaura H, *et al.* Pathophysiological characteristics of the subiculum associated with epileptogenesis in human hippocampal sclerosis. **EBioMedicine** 2018; 29: 38-46.
4. Mutoh H, *et al.* Biallelic variants in *CNPY3*, which encodes an endoplasmic reticulum chaperone, cause early-onset epileptic encephalaopathy. **Am J Hum Genet** 2018; 102: 321-329.
5. Kitaura H, *et al.* Ca^{2+}-permiable AMPA receptors associated with epileptogenesis of hypothalamic hamartoma. **Epilepsia** 2017; 58: e59-e63.
6. Miyake N, et al. Biallelic *TBCD* Mutations Cause Early-Onset Progressing Multiple System Neurodegeneration. **Am J Hum Genet** 2016; 99: 950-61.
7. Tada M, *et al.* Characteristic microglial features in patients with hereditary diffuse leukoencephalopathy with spheroids. **Ann Neurol** 2016; 80: 554-65.
8. Nakashima M, *et al.* Somatic mutations in the *MTOR* gene cause focal cortical dysplasia type IIb. **Ann Neurol** 2015; 78: 375-86.

NETWORKS, STRUCTURE AND CONNECTIVITY IN THE DEVELOPING BRAIN

L-08

David EDWARDS

Centre for the Developing Brain, King's College London, UK

Understanding normal cerebral connectivity in detail will provide insights into fundamental neural processes. By linking structural and functional connectivity to genetic, cognitive and environmental information it will be possible to answer specific neurobiological questions on the creation of mental functions, structure-function relationships, and the influences that shape them. While a complete read of the connectome must incorporate micro-, meso- and macro-scale data, the current state of the art requires that these be considered separately, although within an informatics structure that will facilitate large-scale, probabilistic, integration of data at a later stage. Uniquely and excitingly, the millimeter scale macro-connectome can be studied non-invasively and directly in the foetus and infant by neuroimaging, particularly diffusion Magnetic Resonance Imaging (dMRI) and functional connectivity Magnetic Resonance Imaging (fcMRI). Connectomics, like genomics, requires massive datasets that are comprehended computationally, and open-source neuroinformatic environments for large-scale integration of ever-increasing datasets are at the heart of this new science. These datasets are thus now being accumulated.

CURRICULUM VITAE

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Education

University of Oxford	1974-77
Harvard University, USA	1977-78
Guy's Hospital Medical School, University of London	1978-83

Degrees

B.A. (First Class Honours)	1977
M.B., B.S. (with Distinctions)	1983
D.Sc. (Imperial College London)	2011

Fellowships and Prizes

Open Scholarship, St Peters College, Oxford	1975-7
Sumnos Honores Prize, St Peters College Oxford	1977
Kennedy Scholarship, Harvard University, USA	1977-8
Fellow of the Royal College of Physicians	1993
Fellow of the Royal College of Paediatrics and Child Health	1997
Fellow of the Academy of Medical Sciences	2002
Arvo Ylppo Quinquennial International Gold Metal and Prize (€50,000)	2007
National Institute for Health Research Senior Investigator (renewed)	2008-15
Fellow of the Royal College of Radiologists	2016

Current Appointments

Founding Director, Centre for the Developing Brain, King's College London
The Centre was founded at Imperial College London to develop the work of the successful MRC Clinical Sciences Centre (CSC) Neonatal Medicine Group. The MRC provided funding that allowed the Centre to transfer to a new purpose-built research facility in King's College London, which was formally opened by the Chief Medical Officer, Dame Sally Davies FRS with the Director of the Wellcome Trust, Sir Mark Walport FRS in 2013.
The Centre has 4 full-time, 1 part-time, and 1 honorary professors, and about 90 research staff, and continues to develop, with 3 recently appointed Lecturers and 3 new Senior Lecturers. It conducts bench-to-bedside research focused on neonatal brain injury and neural rescue, as well as active training and public involvement programmes. In addition to grants held by the Director, senior members have obtained programme funding from the Wellcome Trust, the Leducq foundation, and EPSRC.
Professor of Paediatrics and Neonatal Medicine, King's College London
Head of the Department of Perinatal Imaging and Health, King's College London
Group Leader, MRC Centre for Neurodevelopmental Disorders.
Consultant Neonatologist, Guy's and St Thomas' NHS Trust.

Previous Appointments

Weston Professor of Neonatal Medicine, Imperial College	1992-2012
Consultant Neonatologist, Imperial College Healthcare NHS Trust	1992-2012
Head, Division of Paediatrics, Obstetrics and Gynaecology, Imperial College	2001-9
Head, MRC Clinical Sciences Centre Neonatal Medicine Group	2006-12
Founding Associate Director, NIHR Medicines for Children Research Network	2006-13

L-09 USEFULNESS OF MRI REGARDING NEONATAL SEIZURE

Tetsu NIWA

Tokai University School of Medicine, Japan

Neonatal seizure can be caused by various etiology such as hypoxic-ischemic injury, stroke, intracranial hemorrhage, thrombosis, malformation, infection, metabolic disorders, and drug-induced disturbance. MRI can be a useful tool to assess the intracranial status. However, MRI for infants are sometimes difficult for several factors such as small head size and restless at the scanner. Imaging interpretation is sometimes difficult because of changing normal findings with development and obscured clinical onset in some neonates.

Recent advance in MRI can provide faster and detail imaging assessment of infantile brain. Particularly a use of a 3T-MRI provides more detail anatomical information as well as subtle signal-change lesions. Imaging assessment includes brain parenchymal malformation, cystic changes, parenchymal signal abnormalities, hemorrhage, calcification, ventricular form, and the vessels. Knowledge for the MRI findings can be useful for considering the etiology and relating disorders in neonatal seizure.

CURRICULUM VITAE

Education:
1995 M.D. (Medicine), School of Medicine, Yokohama City University
2004 Doctor of Medical Science. (Radiology), School of Medicine, Yokohama City University

Professional experience:
1995- Clinical Resident, Yokohama City University Hospital
1999- Staff Radiologist, Radiology Division, Yokohama City University Medical Center.
2002- Staff Radiologist, Radiology Division, Kanagawa Cancer Center.
2005- Staff Radiologist, Radiology Division, School of Medicine, Yokohama City University.
2006- Staff Radiologist, Radiology Division, Kanagawa Children's Medical Center.
2009- Visiting researcher, Division of Radiology, University Medical Center Utrecht
2010- Staff Radiologist, Radiology Division, Kanagawa Children's Medical Center.
2012- Associate Professor, Tokai University School of Medicine

Specialist:
Japan Radiological Society
The Japanese Society of Interventional Radiology
Japanese Society of Nuclear Medicine

Professional memberships:
Japanese Radiological Society (No.10422)
Japanese Society for Magnetic Resonance in Medicine (No.6388)
Japanese Society of Interventional Radiology (No.1843)
Japanese Society of Nuclear Medicine (No. 11706)
The Japanese Society of Neuroradiology (No. 1109)
Japanese Society of Pediatric Radiology (No.1419)
International society of magnetic resonance in medicine (No.64438)

Award:
- 2008, Silver medal of the 67th annual meeting of Japan Radiological Society Japanese.
- 2008, Certificate of Merit award, 94th Scientific assembly and annual meeting, Radiological Society of North America, Annual Meeting.
- 2009, Best presentation, 20th annual meeting of Japanese society of muscroskeletal radiology, Magnetic resonance imaging findings of a case of scurvy.
- 2009, Kuroki Award, Kanagawa Children's Medical Center.
- 2013, Summa com laude, poster case report. The Japanese Society of Neuroradiology.

Special interests & experience:
- Magnetic resonance imaging
- Pediatric imaging

USEFULNESS OF MRI IN PERINATAL BRAIN INJURIES

L-10

Katsumi HAYAKAWA[1], Koichi TANDA[2], Akira NISHIMURA[3],
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Neonatal hypoxic-ischemic encephalopathy (HIE) may cause significant and life-long neurologic disability. Therapeutic hypothermia has become a standard treatment for neonates with moderate or severe HIE, leading to improvement of overall neurologic outcomes and reducing the incidence of death and disability. MRI assists in defining the nature and extent of HIE. Patterns of brain injury on MRI at 1 week after birth have shown to predict abnormal functional outcome in childhood.

We provide the MRI pattern of HIE of term infants to characterize the extent and severity of brain injury and discuss the role of MRI as a biomarker of neuromotor development. The following issues on MRI finding are discussed; firstly, the correlation of negative pseudonormalization of DWI (residual high signal lesions on DWI beyond the first week) and clinical outcome, secondly, MRI findings of total brain injury, as the new category of HIE caused by prolonged profound asphyxia, shown with the serial MRI findings including day 1-3, second week and after one month of life, thirdly, pontine and cerebellar injury caused by very severe HIE, to characterize MR imaging features of pontine and cerebellar injury and a background HIE pattern and also to assess the clinical outcomes.

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Education
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1968.04.01. Admission to Faculty of Medicine, Kyoto University
1974.03.25. Graduation of Faculty of Medicine, Kyoto University

Licence
1974.05.30. Medical Doctor (No=221112)
1980.06.20. Board Certified Radiologist (No=R03255)
1986.07.25. PhD Kyoto University

History of employment
1974.04.01.-06.30. resident of Kyoto University Hospital
1974.07.01.-1976.03.31. resident at Department of Radiology, Kyoto University Hospital
1976.04.01.-1982.03-6.30. staff at Department of Radiology Kyoto City Hospital
1982-07.01.-1984.06.30. Research fellow at Department of Radiology, University of Rochester. Rochester NY, USA
1984.07.01.-1987.03.31. Lecturer, Fukui Medical School
1987.04.01.-2014.03.31. Director at Department of Radiology, Kyoto City Hospital
2014.04.01.-2017.09.30. Director at Department of Radiology, Iwate Prefectural Kamaishi Hospital
2017.10.01.- present part-time Radiologist at Department of Diagnostic Radiology, Kyoto Red Cross Daiichi Hospital

L-11 NEONATAL SEIZURES AND SODIUM CHANNELOPATHIES

Katherine B. HOWELL

Royal Children's Hospital Melbourne, Australia

Mutations in the sodium channel genes, including SCN2A, are important genetic causes of epilepsy. SCN2A mutations are associated with a number of different clinical phenotypes. They are a major cause of neonatal and early-infantile epilepsy, with a spectrum of severity that spans self-limiting epilepsy with normal development (benign familial neonatal-infantile seizures) to refractory epilepsy with severe developmental impairment (SCN2A encephalopathy), and can also cause epilepsy with onset in mid-infancy (with infantile spasms) or childhood, and a phenotype of intellectual disability/autism without epilepsy. The distinct phenotypes appear to correlate with the molecular effects (gain- or loss- of function) of the mutations. This talk will discuss the clinical and molecular phenotypes of SCN2A mutations, with a focus on the neonatal presentations and their treatment implications.

CURRICULUM VITAE

Dr Katherine Howell is a paediatric neurologist and epileptologist at the Royal Children's Hospital and a Clinician-Scientist Fellow at the Murdoch Children's Research Institute in Melbourne, Australia. Her current areas of research focus are severe epilepsies of infancy, infantile spasms, genetic epilepsies and *SCN2A*-related disorders. She is the lead investigator on an international *SCN2A* natural history study. Her work is supported by the National Health and Medical Research Council of Australia, and biotechnology company, RogCon Biosciences, Inc.

Select publications include:

1. **Howell KB**, Eggers S, Dalziel K, Riseley J, Mandelstam S, Myers CT, McMahon JM, Schneider A, Carvill GL, Mefford HC, Victorian Severe Epilepsy of Infancy Study Group, Scheffer IE, Harvey AS. An epidemiological and cost-effectiveness study of early genetic testing in severe epilepsies of infancy. *Epilepsia 2018*.

2. #McTague A, #**Howell KB**, Cross JH, Kurian MA, Scheffer IE. The genetic landscape of the epileptic encephalopathies of infancy and childhood. Lancet Neurology, 2015; 15:304-316 #These authors contributed equally

3. **Howell KB**, McMahon JM, Carvill GL, Tambunan D, Mackay MT, Rodriguez-Casero V, Webster R, Clark D, Freeman JK, Calvert S, Olson HE, Mandelstam S, Poduri A, Mefford HC, A Simon Harvey, Scheffer IE. *SCN2A* encephalopathy: a major cause of epilepsy of infancy with migrating focal seizures. Neurology, 2015; 85:958-966

4. Berecki G, **Howell KB**, Deerasooriya YH, Cilio MR, Kaplan D, Scheffer IE, Berkovic SD, Petrou S. Dynamic clamp modelling predicts functional separation in mild familial and severe de novo forms of *SCN2A* epilepsy. *PNAS 2018*.

GENETIC ETIOLOGY OF NEONATAL EPILEPSIES BY CAUSES OTHER THAN ABNORMALITIES OF SODIUM ION CHANNELS

L-12

Atsushi ISHII

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

One of the causes of epilepsy is an imbalance between the central nervous system excitation and inhibition. Ion channels, including ligand-gated ion channels, play an important role in directly controlling neuronal excitation and inhibition. In fact, many abnormalities of sodium- or potassium- ion channels or $GABA_A$ receptors have been linked to epilepsy. Sodium ion channels mainly contribute to neuronal excitation, and potassium ion channels and $GABA_A$ receptors contribute to inhibition. Here, we focus on the genes, which encode potassium ion channels (*KCNQ2*, *KCNA2*, and *KCNT1*) and $GABA_A$ receptors (*GABRA1*, *GABRB2*, and *GABRB3*), which contribute to the inhibition of nerve cells, and highlight especially their relationship with neonatal epilepsy.

Self-limited (familial) neonatal epilepsy (SL(F)NE) and epileptic encephalopathies are caused by the abnormalities of the *KCNQ2*, which encode the subunits of the voltage gated K^+ channels. Pathogenic variants of the *KCNQ2* for SL(F)NE cause haploinsufficiency. On the other hand, most pathogenic variants in epileptic encephalopathies cause dominant-negative effects.

Abnormalities of the *KCNA2*, which encodes Shaker-related voltage-gated K^+ channels cause the gain- and loss-of-function for neonatal onset.

KCNT1 encodes the sodium-activated K^+ channels. Pathogenic variants have been linked to Ohtahara syndrome as well as epilepsy during infancy with migrating focal seizures.

$GABA_A$ receptors, composed of pentamers of $\alpha 1$, $\beta 1/2/3$ and $\gamma 2$ subunits, suppress neuronal excitation by inhibiting neurotransmission. Pathogenic variants in each of the subunit have been found in patients with febrile seizures to epileptic encephalopathies. Therefore, it is still difficult to accurately predict the etiologic gene from the onset age.

CURRICULUM VITAE

Atsushi Ishii, M.D, Ph.D.
Associate Professor, Department of Pediatrics, School of Medicine, Fukuoka University

2001	BS. Kyoto Pharmaceutical University
2007	M.D. Fukuoka University, School of Medicine
2007-2008	Resident, National Hospital Organization, Kanmon Medical Center
2008-2009	Resident, Yamaguchi University Hospital
2009-2010	Clinical Fellow in Pediatrics, Fukuoka University Hospital
2010-2011	Clinical Fellow in Pediatrics, Kyusyu Kosei Nenkin Hospital
2011-2013	Clinical Fellow in Pediatrics, Fukuoka University Hospital
2013	Ph.D. Fukuoka University, School of Medicine
2013-2014	Postdoctoral Scholar in Center for Human Genome Variation, School of Medicine, Duke University
2014-2016	Postdoctoral Scholar in University of Arizona Genetics Core, University of Arizona
2016-2017	Medical director in Pediatrics, Miyakonojo Medical Association Hospital
2017-2019	Assistant Professor in School of Medicine, Fukuoka University
2019-present	Associate Professor in School of Medicine, Fukuoka University

Society for Neuroscience (USA), The Japan Society Human Genetics, The Japanese Society of Pediatrics, The Japanese Society of Child neurology, Japanese Society for Epilepsy, American Society for Epilepsy. Member of Japanese Febrile seizures guideline. Councilor of Infantile Seizure Society

L-13

GENE PANEL ANALYSIS IN NEONATAL / INFANTILE EPILEPTIC ENCEPHALOPATHY: PERSPECTIVE FROM A PAEDIATRIC NEUROLOGIST

Cheuk Wing FUNG

Division of Neurology, Department of Paediatrics and Adolescent Medicine,
Hong Kong Children's Hospital, Hong Kong

Epileptic encephalopathy (EE) is a heterogeneous condition causing deteriorations of cognitive, motor and/or sensory functions as a consequence of epileptic activities. It is the most common and severe in infancy and early childhood. Molecular diagnosis of patients with EE is challenging due to genetic and phenotypic heterogeneity of numerous monogenic disorders. Next generation sequencing (NGS) is therefore a very powerful tool for molecular workup of these patients. For EE with neonatal / infantile onset, the diagnostic yield could be as high as 50 to 60%. This talk will cover the clinical approach and use of gene panel analysis in NGS in the workup for patients with neonatal / infantile EE, including recent advances to further improve the diagnostic accuracy.

CURRICULUM VITAE

Dr Cheuk-wing FUNG graduated from the University of Hong Kong. His interest in child neurology started shortly after he joined Queen Mary Hospital, Hong Kong in 1996. Dr Fung had a 1-year overseas training in Great Ormond Street Hospital for Sick Children (London) from 2003 to 2004, with particular focus on neurometabolic diseases, epilepsy and acute neurology. Currently, he is the Associate Consultant of the Department of Paediatrics in Hong Kong Children's Hospital, Honorary Clinical Assistant Professor of the University of Hong Kong, Vice-president of the Paediatric Neurology Association of Hong Kong and Vice-president of the Hong Kong Society for Inborn Error of Metabolism. His main area of clinical research is neurometabolic, in particular mitochondrial diseases, and neurodegenerative diseases. Recently, he has finished a 6-month training in the Radboud Centre for Mitochondrial Medicine, Nijmegen, the Netherlands in 2015.

NEUROPHYSIOLOGICAL ASPECTS OF NEONATAL SEIZURES

L-14

Geraldine B. BOYLAN

INFANT Centre, University College Cork, Ireland

Neonatal seizures are the most common neurological emergency in the neonatal intensive care unit (NICU). Modern digital technology has enabled monitoring of both premature and full term newborn infants in the NICU with continuous uninterrupted multichannel EEG for days at a time. As a result, detailed characteristics of neonatal seizures are now available. Acute neonatal seizures occur soon after birth in infants and are commonly caused by hypoxia, ischaemia, infection, stroke and haemorrhage.

This presentation will outline the neurophysiological characteristics of neonatal seizures in both term and preterm infants. Features such as location, time of onset, seizure burden, peak intensity will be presented using multiple illustrations. Following hypoxia ischaemia, seizures evolve in a specific way and this is influenced by hypothermia treatment. Commonly used antiepileptic drugs can abolish neonatal seizures permanently or temporarily and the pattern of electrographic seizure response will be discussed. There is accumulating evidence on the impact that a high electrographic seizure burden can have on neurodevelopmental outcome and current research in this area will be presented. Finally, the importance of the background EEG pattern in infants with seizures will be highlighted.

CURRICULUM VITAE

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EDUCATION AND PROFESSIONAL QUALIFICATIONS:
2008 - MA (Education), UCC.
2002 - PhD in Clinical Medicine, University of London.
1991 - MSc (Comparative Physiology), University of London.
1989 - BSc (Physiology), University of London.

CURRENT POSITION:
April 2013 – 2017: Director, INFANT Research Centre, University College Cork, IRELAND
June 2009 – Present: Professor of Neonatal Physiology, Department of Paediatrics and Child Health, University College Cork.

SELECTED PUBLICATIONS: Full publication list available at https://orcid.org/0000-0003-0920-5291

Rennie JM, de Vries LS, Blennow M, Foran A, Shah DK, Livingstone V, van Huffelen AC, Mathieson SR, Pavlidis E, Weeke LC, Toet MC, Finder M, Pinnamaneni RM, Murray DM, Ryan AC, Marnane WP, Boylan GB. Characterisation of neonatal seizures and their treatment using continuous EEG monitoring: a multicentre experience. Arch Dis Child Fetal Neonatal Ed. 2018 Nov 24. pii: fetalneonatal-2018-315624.

O'Sullivan MP, Looney AM, Moloney GM, Finder M, Hallberg B, Clarke G, Boylan GB, Murray DM. Validation of Altered Umbilical Cord Blood MicroRNA Expression in Neonatal Hypoxic-Ischemic Encephalopathy. JAMA Neurol. 2018 Dec 28. doi: 10.1001/jamaneurol.2018.4182.

Soul JS, Pressler R, Allen M, Boylan G, Rabe H, Portman R, Hardy P, Zohar S, Romero K, Tseng B, Bhatt-Mehta V, Hahn C, Denne S, Auvin S, Vinks A, Lantos J, Marlow N, Davis JM; International Neonatal Consortium. Recommendations for the design of therapeutic trials for neonatal seizures. Pediatr Res. 2018 Dec 24. doi: 10.1038/s41390-018-0242-2.

Dempsey EM, Kooi EMW, Boylan G. It's All About the Brain-Neuromonitoring During Newborn Transition. Semin Pediatr Neurol. 2018 Dec;28:48-59. doi: 10.1016/j.spen.2018.05.006.

Finn D, O'Toole JM, Dempsey EM, Boylan GB. EEG for the assessment of neurological function in newborn infants immediately after birth. Arch Dis Child Fetal Neonatal Ed. 2018 Nov 26. pii: fetalneonatal-2018-315231.

O'Shea A, Lightbody G, Boylan G, Temko A. Investigating the Impact of CNN Depth on Neonatal Seizure Detection Performance. Conf Proc IEEE Eng Med Biol Soc. 2018 Jul;2018:5862-5865.

Goulding, R. M., Stevenson, N. J., Murray, D. M., Livingstone, V., Filan, P. M., & Boylan, G. B. (2017). Heart rate variability in hypoxic ischemic encephalopathy during therapeutic hypothermia. Pediatr Res. 81(4):609-615.

Ahmed, R., Temko, A., Marnane, W., Lightbody, G., & Boylan, G. (2016). Grading hypoxic–ischemic encephalopathy severity in neonatal EEG using GMM supervectors and the support vector machine. Clinical Neurophysiology, 127(1), 297-309.

Lloyd, R. O., O'Toole, J. M., Livingstone, V., Hutch, W. D., Pavlidis, E., Cronin, A. M., & Boylan, G. B. (2016). Predicting 2-y outcome in preterm infants using early multimodal physiological monitoring. Pediatr Res. 80(3):382-8.

Mathieson, S. R., Stevenson, N. J., Low, E., Marnane, W. P., Rennie, J. M., Temko, A., Lightbody, G., & Boylan, G. B. (2016). Validation of an automated seizure detection algorithm for term neonates. Clinical Neurophysiology 127(1), 156-168.

Murray, D. M., O'Connor, C. M., Ryan, C. A., Korotchikova, I., & Boylan, G. B. (2016). Early EEG Grade and Outcome at 5 Years After Mild Neonatal Hypoxic Ischemic Encephalopathy. Pediatrics 138(4) Pressler R, Boylan GB, Marlow N et al. (2015). Bumetanide for the treatment of seizures in newborn babies with hypoxic ischaemic encephalopathy (NEMO): an open-label, dose finding, and feasibility phase 1/2 trial. Lancet Neurol. 14(5):469-77.

Stevenson NJ, Clancy RR, Vanhatalo S, Rosén I, Rennie JM, Boylan GB. (2015). Interobserver agreement for neonatal seizure detection using multichannel EEG. Ann Clin Transl Neurol.1;2(11):1002-11.

An Automated System for Grading EEG Abnormality in Term Neonates with Hypoxic-Ischaemic Encephalopathy N. J. Stevenson, I. Korotchikova, A. Temko, G. Lightbody, W. P. Marnane, G. B. Boylan. (2013). Annals of Biomedical Engineering. Volume 41, Issue 4, pp 775-785.

Temko A, Thomas E, Marnane W, Lightbody G, Boylan GB. (2011). Performance assessment for EEG-based neonatal seizure detectors. Clin Neurophysiol. 122(3):474-82.

L-15 BASIC RESEARCH ON PHYSIOLOGY OF FETAL-NEONATAL BRAIN

Sampsa VANHATALO

Children's Hospital, Helsinki University Hospital, Finland

Prof Sampsa Vanhatalo has EU qualification (board exam) as a clinical neurophysiologist, and he is the professor and senior consultant in clinical neurophysiology in Helsinki University Hospital. He obtained his MD and PhD degrees in 1998 from the University of Helsinki, Finland, and he also has clinical experience in general practice, pediatrics, pediatric neurology, epileptology, neurology, and emergency medicine.

Dr. Vanhatalo is leading the BABA center in Helsinki Children's Hospital, dedicated to studies on baby brain activity (www.babacenter.fi). For the past fifteen years, he has focused on developing methodology for neonatal neurophysiology ranging from the development of EEG hardware to other devices (eg. EEG caps and stimulators), mathematical signal analyses, as well as neurobiological models underlying early EEG activity. Most recently, Vanhatalo's group has initiated projects to develop medical wearables for the mobile assessment of infant sleep and mobility. All these activities have a heavy translational emphasis whereby the targets of research have been set to result in medical applications, and hence ultimately benefit clinical work and ill babies.

CLINICAL MANIFESTATIONS OF NEONATAL SEIZURES

L-16

Courtney J. WUSTHOFF

Stanford University, USA

Neonatal seizures may have challenging presentations. This session will discuss current dilemmas in diagnosis and evaluation of neonatal seizures. An overview of clinical manifestations of neonatal seizures will be given, including a comparison of historical and proposed neonatal seizure classification systems. The problem of subtle or subclinical neonatal seizures will be considered in detail. Recent data regarding which populations are at highest risk will be summarized, to facilitate identification of those neonates that might benefit from screening for seizures using brain monitoring tools. Finally, this session will evaluate current evidence regarding the potential benefits and drawbacks of various neurophysiologic tools for diagnosis, including conventional EEG and amplitude-integrated EEG.

CURRICULUM VITAE

Contact Information Stanford University Division of Child Neurology 750 Welch Road, Suite 317 Palo Alto, CA 94304
wusthoff@stanford.edu
650-736-0885

Education

9/2012-1/2014 MS Stanford University- School of Medicine Epidemiology and Clinical Research

9/2000-6/2004 MD University of California, San Francisco- School of Medicine

9/1996-5/2000 BA Columbia University, New York, NY Columbia College - Neuroscience & Behavior (Magna Cum Laude)

Postgraduate Training

7/2009- 6/2010 Children's Hospital of Philadelphia Epilepsy & Clinical Neurophysiology Fellowship

7/2006- 6/2009 Children's Hospital of Philadelphia & Hospital of the University of Pennsylvania Child Neurology Residency Training Program

7/2004-6/2006 Children's Hospital and Research Center at Oakland Pediatrics Residency Training Program

Appointments

9/2012-current Assistant Professor of Neurology and Neurological Sciences Division of Child Neurology, and by courtesy, Pediatrics-Neonatal and Developmental Medicine, Stanford University

7/2010-7/2012 Locum Consultant- Neonatal Neurology Division of Neonatology, Imperial College Healthcare NHS Trust

7/2010- 7/2012 Visiting Researcher Division of Clinical Sciences, Imperial College London

Licensure California, Hawaii

Board Certification/Specialist Qualifications

Diplomate, American Board of Psychiatry and Neurology
- Neurology with Special Qualification in Child Neurology
- Epilepsy

Diplomate, American Board of Pediatrics
-General Pediatrics

Diplomate, American Board of Clinical Neurophysiology
- Clinical Neurophysiology
- with added Competency in Epilepsy Monitoring

Awards and Honors

2008 AAN Neurologist-In-Training Clinical Ethics Elective

2008 Stokes Institute Research Poster Award (Patient-Oriented Research)

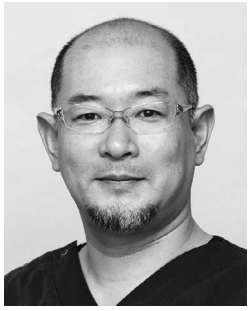
2003 John Conley Prize in Ethics

2002 French Foundation Medical Student Award

2001 John Conley Prize in Ethics

L-17

APPLICATION OF NEW NEONATAL SEIZURE CLASSIFICATION



Tetsuo KUBOTA

Department of Pediatrics, Anjo Kosei Hospital, Japan

Based on the International League Against Epilepsy (ILAE) position on the classification of seizures in this age group, The ILAE Task Force on Neonatal Seizures created a new neonatal seizure classification.
This includes a diagnostic framework for seizures in the neonatal period, including the classification of seizures and a framework for neonatal seizures.
I think that this guideline is clear, rational, and very practical, although the task involved hard work on a challenging topic.
The neonatal seizure classification in the 1950s was based only on direct clinical observations.
Recently, using electroencephalography (EEG)-video analysis of electro-clinical correlations, the American Clinical Neurophysiology Society defined three types of neonatal seizure: (1) clinical-only seizures, (2) electro-clinical seizures, and (3) EEG-only seizures. Neonatal EEG seizures are described as having (1) a sudden EEG change, (2) repetitive waveforms that evolve in terms of morphology, frequency, and/or location, (3) an amplitude of at least 2 μV, and (4) a duration of at least 10 seconds.
The perfect neonatal EEG classification is difficult to establish. Our knowledge of neonatal seizures is increasing. How do we deal with spasms of shorter durations? Are brief interictal rhythmic discharges (BIRDs) equivalent to a seizure that should be treated with antiepileptic drugs? Are neonatal seizures exclusively of focal onset?
In this presentation, I will try to apply this new neonatal seizure classification to our patients and discuss some issues to be solved.

CURRICULUM VITAE

Present position
Chief, Children's Medical Center, Anjo Kosei Hospital

Education
1990-1996 Nagoya University School of Medicine
2000-2003 Ph.D., Pediatric Neurology, Nagoya University Graduate School of Medicine

Appointments
1996-1997 Intern, Anjo Kosei Hospital
1997-1998 Resident, Pediatrics, Anjo Kosei Hospital
1998-2000 Clinical fellow, Pediatrics, Anjo Kosei Hospital
2001-2003 Research fellow in Department of Sensory-Motor Integration, National Institute for Physiological Sciences
2003- Clinical fellow, Department of Pediatrics, Anjo Kosei Hospital

NEONATAL EPILEPSIES: A PRACTICAL APPROACH

L-18

Rhea Angela SALONGA-QUIMPO

Section of Pediatric Neurology, Department of Neurosciences, University of the Philippines-Philippine General Hospital, Phillipines

Neonatal seizures are often symptomatic in nature and due to an underlying brain injury. It is important to distinguish neonatal-onset epilepsies from symptomatic seizures in neonates. Neonatal epilepsies range from the benign familial neonatal epilepsy to the extreme end of the spectrum, which includes neonatal epileptic encephalopathies. The essential features that have to be considered in making the diagnosis of neonatal epilepsies include family history, seizure semiology, clinical presentation, and interictal and ictal EEG patterns. Ancillary information that may contribute to the diagnosis of neonatal epilepsies include metabolic screening and imaging studies. Genetic testing may confirm the diagnosis of specific neonatal epilepsies. Differentiating the etiology of neonatal epilepsies is a key factor in deciding appropriate treatment. The treatment of neonatal epilepsies in the past was generic, with no consideration of etiology. With the current understanding of neonatal epilepsies, treatment has moved towards precision medicine with specific targeted therapy for certain epilepsy syndromes.

CURRICULUM VITAE

Dr. Rhea Angela Salonga-Quimpo is a Pediatric Neurologist and Epileptologist. She obtained her medical degree from the University of the Philippines College of Medicine. She then pursued training in Pediatric Neurology at the University of Chicago Medical Center in Chicago, Illinois and underwent a Fellowship in Clinical Neurophysiology, EEG and Epilepsy at the Cleveland Clinic in Ohio. She returned to her home country, the Philippines in late 2013. Since then, Dr. Salonga-Quimpo has been actively involved in epilepsy advocacy in the Philippines. She is currently a Clinical Associate Professor at the Department of Neurosciences, University of the Philippines College of Medicine and Philippine General Hospital. She is a member of the Epilepsy Council of the Philippine Neurological Association. She is also an active member of the Philippine League Against Epilepsy. She has lectured both locally and internationally on various topics and issues in Pediatric Epilepsy.

L-19 INBORN ERRORS OF METABOLISM IN NEONATAL SEIZURES

Derrick Wei-shih CHAN

KK Women's and Children's Hospital, Singapore

Neonatal seizures are a unique entity. They differ from seizures occurring at other times of life in terminology, semiology and aetiology. Seizures can occur in approximately 0.5% of term neonates and up to 22.2% of pre-term neonates. Neonatal seizures have a many possible aetiologies and are most commonly symptomatic due to neonatal encephalopathy (60%), intracranial infection (5-10%), intracranial haemorrhage, developmental malformations and correctable metabolic disturbances such as hypoglycaemia and derangement of electrolytes (e.g. sodium, calcium and magnesium). Once these common aetiologies have been excluded or seem unlikely, it is important to consider rarer causes including inborn errors of metabolism.

We will discuss recognizable neonatal epileptic encephalopathies and their aetiologies, as well as inborn errors of metabolism that present with neonatal encephalopathy and/or seizures and an approach to evaluation and management.

CURRICULUM VITAE

I am a Senior Consultant and Head of Paediatric Neurology at KK Women's and Children's Hospital. I graduated from Nottingham University with Bachelor's in Medical Science (1996) and Bachelor of Medicine and Surgery (1998), passed my Membership exams for the Royal College of Paediatrics and Child Health in 2002 and obtained Specialist Accreditation in Paediatric Medicine in 2007. I trained in Paediatric EEG at Great Ormond Children's Hospital in London, UK and the Royal Children's Hospital in Melbourne, followed by Clinical Fellowship in Paediatric Epilepsy at the Hospital for Sick Children in Toronto. I obtained certification in Clinical Neurophysiology from the Canadian Society of Clinical Neurophysiology in 2008 and received my Master's Degree in Clinical Investigation in 2011. I set up the comprehensive epilepsy programme at KKH, including the epilepsy monitoring unit, ketogenic diet and complicated epilepsy clinics, vagus nerve stimulator implantation programme and epilepsy surgery programme. I am driving the paediatric epilepsy research programme and have established collaborations in Paediatric Epilepsy with Duke Durham. I have led the Paediatric Neurology team to clinical, research and educational excellence, expanding the team and establishing expertise in vital areas of paediatric neurology. I am an instructor and examiner for the ASEAN Epilepsy Academy (ASEPA) Electro-encephalography exam.

I have research interests in video analytics for seizure detection and HLA-B*1502 alleles in children with carbamazepine hypersensitivity. I am currently PI of NMRC HSRG grant "HSRG-OC17Jun: Cost containment in pharmacogenomic testing, identifying obstacles to implementation of pharmacogenomics and impact on anticonvulsant prescription patterns". I set up the Paediatric Autoimmune Epilepsy, Demyelination & Encephalitis Study (PAEDES) under the KKH NMRC Centre grant and have conducted translational research in close collaboration with Prof Salvatore Albani and the Singhealth/Duke-NUS Translational Immunology Institute. I am developing the Clinician Innovator track in Singhealth with A/Prof Henry Ho. As Vice-Chair (Research) for the Paediatrics ACP.

TREATMENT AND EEG MONITORING FOR NEONATAL SEIZURES

L-20

Ronit PRESSLER

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

Neonatal seizures are the most common expression of brain injury in neonates. Accurate diagnosis of neonatal seizures is challenging. Both over and under-diagnosis of neonatal seizures remain a frequent problem because many neonatal behaviours may resemble seizures and most electroencephalography (EEG)-confirmed seizures have only subtle clinical signs or are entirely subclinical. It is clear, however, that prompt seizure treatment is important, because when seizures are prolonged, they become more and more difficult to abort. Therefore, accurate seizure diagnosis requires brain monitoring with either conventional or amplitude-integrated electroencephalography (aEEG). Timely recognition and effective treatment of neonatal seizures is recommended in order to mitigate secondary seizure-induced brain injury and improve long term neurological outcomes, but the choice of seizure treatment threshold remains a matter of debate. Phenobarbital remains the first line choice worldwide even though systemic reviews have shown that there is little evidence base regarding its efficacy and long term safety. Second line choice varies considerable within and between countries with even less evidence for efficacy. These include phenytoin, levetiracetam, benzodiazepines, and lidocaine. If inborn errors of metabolism are suspected as aetiology trial of pyridoxine, pyridoxal-5-Ph phosphate, folate and biotin should be considered. There is an urgent need for efficient and successful drug trials of both old and new drugs to improve the treatment and outcome for this highly vulnerable population.

CURRICULUM VITAE

Ronit is Consultant in Clinical Neurophysiology and clinical lead of the Telemetry Unit at Great Ormond Street Hospital for children, London and Associated Professor at the UCL-Institute of Child Health. She qualified from Berlin University in 1992 and trained in paediatrics in Berlin, Germany and clinical neurophysiology at the National Hospital for Neurology and Neurosurgery, London, obtaining her MD in 1997 and her PhD in 2006.
Her research interests include neonatal seizures, particularly their diagnosis and treatment, as well as the effect of epilepsy on cognition and pre-surgical evaluation in children with complex epilepsy. Since 2015 she has been on the council of the British Society for Clinical Neurophysiology BSCN) and currently severs as meeting secretary. She is also affiliated member of the Paediatric Neuroscience Clinical Reference Group, NHS England. She is chair of the ILAE neonatal seizure classification task force as well as co-chair of the ILAE neonatal guidelines and the INC Neonatal seizure working group.

L-21 ANTIEPILEPTIC TREATMENT FOR NEONATAL SEIZURES

Akihito TAKEUCHI

Division of Neonatology and Neuropediatrics, National Hospital Organization Okayama Medical Center, Japan

Adequate treatment for neonatal seizures is vitally important because of potential adverse effects of seizures on the developing brain. There remains, however, uncertainty as to the optimal management of neonatal seizures, owing to a lack of extensive evidence-based information.

In the first part of this lecture, I will review the usage of antiepileptic agents for neonatal seizures. Representative neonatal seizure management algorithms, which were recently suggested, recommend phenobarbital as the first-line agent, and phenytoin (PHT)/fosphenytoin (FOS) and levetiracetam as the second-line agents. However, most antiepileptic medications have adverse effects on cardiac function, blood pressure, and ventilation. From a neonatologist´s perspective, these adverse effects might disturb the practice of intensive care. Thus, I will also outline the adverse effects of these antiepileptic medications.

In the second part of this lecture, I will refer to the efficacy of Na-channel blockers for KCNQ2-related neonatal epilepsy. The effectiveness of PHT and carbamazepine (CBZ) for KCNQ2 encephalopathy and the efficacy and safety of low-dose oral CBZ in benign familial neonatal epilepsy were recently reported. We also observed the efficacy of FOS and CBZ in cases of non-familial neonatal epilepsy with KCNQ2 mutation, which is suspected from clinical information, such as postnatal days of seizure onset, characteristic initial brief period of EEG flattening accompanied by apnea, and no significant abnormal findings of brain imaging and metabolic tests. If KCNQ2-related neonatal epilepsy is suspected from clinical information including family history, it is better to assign priority to the administration of PHT/FOS and CBZ.

CURRICULUM VITAE

Training History and Professional Career

2003 Junior resident, Department of Pediatrics, National Hospital Okayama Medical Center
2005 Senior resident, Division of Neonatology, National Hospital Organization Okayama Medical Center
2007 Clinical fellow, Department of Child Neurology, Okayama University Hospital
2011 Staff doctor, Division of Neonatology, National Hospital Organization Okayama Medical Center
2017 Staff doctor, Division of Neonatology and Neuropediatrics, National Hospital Organization Okayama Medical Center

Degree

2003 Diploma of Medicine (Mie University, Japan)
2013 Doctor of Philosophy (Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Science, Japan)

Qualification

2003 Medical License (Japan)
2010 Board Certified Pediatrician (Japan Pediatric Society)
2013 Board Certified Child Neurologist (The Japanese Society of Child Neurology)
2016 Board Certified Neonatologist (Japan Society of Perinatal and Neonatal Medicine)

Social activity

2015 Member of the Baby Cooling Japan Working Group
2016 Manager of Neonatal Care Forum Mailing List
2017 Councilor of the Japanese Society of Child Neurology

Award

2011 Excellent Poster Award for Young Investigator, The 53th Annual Meeting of the Japanese Society of Child Neurology
2017 Japan Eli Lilly Award, Japan Foundation for Pediatric Research
2017 The Best Paper Awards, Japanese Society of Child Neurology

HYPOTHERMIA FOR NEONATAL SEIZURES

L-22

Jun SHIBASAKI

Department of Neonatology, Kanagawa Children's Medical Center, Kanagawa, Japan

Hypoxic-ischemic encephalopathy is a common cause of seizures in neonates. There is some evidence that therapeutic hypothermia may reduce electrographic seizure exposure in neonates after hypoxic-ischemic encephalopathy. Several single-center, observational studies have recently compared data on conventional EEG in cooled and non-cooled newborn infants with hypoxic-ischemic encephalopathy, and all have shown a potent anticonvulsant effect of hypothermia. In the cooled population with hypoxic-ischemic encephalopathy, a lower seizure burden and a lower incidence of seizure were reported. Animal studies also have shown a reduction in amplitude and extent of seizures. Hypothermia might have an anticonvulsant effect by inhibiting the release of glutamate and free oxygen radicals, and reducing cytotoxic edema. However, comparing seizure incidence on studies conducted before and after therapeutic hypothermia utilization may not reflect a reduction in seizures because most studies performed initially relied on clinical observation for seizure identification while most studies performed later used EEG monitoring for seizure identification. EEG monitoring is the gold standard for detecting all seizures in neonates and this is even more critical in neonates who are cooled. Because they are often sedated, the majority of seizures in neonates undergoing therapeutic hypothermia remain subclinical, making seizures more difficult to detect. Amplitude-integrated EEG monitoring is useful but shorter duration seizures are more likely to be missed. Multiple animal and human studies suggest that seizures exacerbate existing cerebral injury. Therefore, recent guidelines suggest that centers performing therapeutic hypothermia in neonates with hypoxic-ischemic encephalopathy have either aEEG or conventional EEG available for seizure identification.

CURRICULUM VITAE

Name: Dr. Jun Shibasaki MD, Yokohama, Japan

Education:
2000 Graduated from Osaka City University School of Medicine

Professional Training and Employment:
2000-2002 Trained in Paediatrics and Neonatal Medicine in Kanagawa Children's Medical Center
2002-2003 Residency program at the Division of Pediatrics in Fujisawa City Hospital 2003-2005 Residency program at the Division of Neonatology in Kanagawa Children's Medical Center
2005- A staff neonatologist in the Kanagawa Children's Medical Center

L-23

THE NEOLEV2 TRIAL. WHAT HAVE WE LEARNED ABOUT THE MANAGEMENT OF NEONATAL SEIZURES?

Suzanne L. DAVIS

Starship CHildren's Hospital, New Zealand

The choice of a drug treatment for neonatal seizures will balance the risk of harm from ongoing seizures against drug-related adverse effects. Phenobarbital (PB), the standard drug for neonatal seizures, has significant adverse effects. LEV is well tolerated, safe, has a high therapeutic index and low protein binding. We have completed a Phase 2b randomised controlled trial of PB versus levetiracetam (LEV) for first line treatment of neonatal seizures.

NEOLEV2 trial included 280 term neonates suspected of having seizures, or were considered to be at risk of seizures. When electrographic seizures were detected on continuous video-EEG monitoring (106 infants), patents were randomised to receive study drug, PB 20 mg/kg (42) or LEV 40 mg/kg (64). If a further seizure was detected they received 20 mg/kg PB (20) or 20 mg/kg LEV (50). If seizures continued, patients were switched to the alternate drug regimen. In 81 patients treatment was managed according to protocol.

The primary outcome, cessation of seizures for 24 hours, was met by 24 patients (80.0%) who received PB and 15 patients (28.3%) patients who received LEV ($p<0.001$). Adverse effects were reported more frequently in patients who received PB compared to those who received LEV. The higher rate of adverse effects occurred for hypotension, respiratory symptoms and use of pressor agents.

Conclusions from this trial confirm that PB remains the drug of choice for seizure status in the newborn, but LEV could be considered when the overall seizure burden is low.

CURRICULUM VITAE

EDUCATION
1971 BMedSc University of Otago, New Zealand
1972 MBChB University of Otago, New Zealand
1993 PhD University of Auckland, New Zealand

TRAINING
1973-4 House Surgeon, Auckland Hospital and National Women's Hospital, Auckland, New Zealand.
1975 Registrar, Waikato Hospital, Hamilton, New Zealand
1975-7 Resident in Neurology, Washington University, St Louis, MO, USA
1978-9 Fellow in Child Neurology, Washington University, St Louis, MO, USA
1979-80 Fellow in Clinical Neurophysiology, Harvard University, Boston, MA, USA

SPECIALIST CERTIFICATION
1980 American Board of Psychiatry and Neurology, with Special Competence in Child Neurology
1982 American Board of Clinical Neurophysiology

MEDICAL LICENCE
1972 New Zealand, 7674
1979 Missouri
1980 California, A35721

PROFESSIONAL AND ACADEMIC EXPERIENCE
1980-1984 Assistant Professor, Neurology and Pediatrics, University of California San Francisco,
1984-1988 Assistant Professor, Neurology and Pediatrics, University of California Davis
1988-1989 Associate Professor, Neurology and Pediatrics, University of California Davis
1989-2000 Senior Lecturer, Department of Paediatrics, University of Auckland, New Zealand
1989-1992 National Child Health Research Foundation, Senior Research Fellow, University of Auckland, New Zealand
1991-2000 Specialist, Paediatric Neurology, Auckland Children's Hospital, New Zealand
1992-1994 Specialist, Clinical Neurophysiology, Auckland Hospital, New Zealand
1993-1995 Subdean Research and Graduate Studies, School of Medicine, University of Auckland, New Zealand
1995-1997 Assistant Dean Graduate Studies, School of Medicine, University of Auckland, New Zealand
1998-1999 Assistant Dean Post-entry Medical Education, School of Medicine, University of Auckland, New Zealand
2000-2010 Specialist, Child Neurology, Children's Hospital Oakland, Oakland, CA, USA
2010- Specialist, Paediatric Neurology, Starship Children's Health, Auckland, New Zealand
2014 -2016 Specialist, Paediatric Neurology, Wellington Hospital, Wellington, New Zealand

APPROACH TO NEONATAL SEIZURES AT A TERTIARY HOSPITAL IN TURKEY

L-24

Dilek YALNIZOGLU

Hacettepe University Faculty of Medicine, Turkey

Seizures are the most common clinical sign of cerebral dysfunction in neonatal period. Underlying etiology is related with the neurological outcome, including a wide range of cognitive and motor impairment, as well as future epilepsy. Hypoxic-ischemic encephalopathy is the leading cause for neonatal seizures.

Initial approach to newborns with seizures is treatment of seizures and prompt evaluation to determine the etiology. Treatment of seizures along with the diagnosis and management of underlying cause(s) are crucial. Neonatal/infantile metabolic epilepsies and genetic epilepsies should be considered in the differential diagnosis of refractory cases particularly when family history and parental consanguinity are present. EEG is helpful in detecting the background activity and electrographic seizures both in newborns with clinical seizures and newborns with high risk for seizures.

The antiseizure medication preferences at our institution is similar with the conventional treatment approach in the literature. Phenobarbital is considered the first line antiseizure medication; phenytoin may be used as a second or third choice of treatment. Both oral and intravenous formulations of levetiracetam are used. Midazolam, as a continuous drip is the treatment of choice for patients refractory to other medications. Topiramate is used as another option in newborns who can tolerate oral formulations, if seizures persist despite initial treatment.

CURRICULUM VITAE

Dilek Yalnizoglu, MD
Hacettepe University Faculty of Medicine
Department of Pediatric Neurology
Ankara, Turkey

Dilek Yalnizoglu is a Professor in Pediatrics, and Pediatric Neurologist/Epileptologist at Hacettepe University Children's Hospital Department of Pediatric Neurology in Ankara, Turkey. Dr. Yalnizoglu received her MD degree in 1989 at Ankara University Medical School in Ankara, Turkey. She completed her pediatric residency in 1994, and pediatric neurology fellowship in 1997, both at Hacettepe University Children's Hospital, Ankara. She completed her training in Clinical Neurophysiology and Epilepsy between 1997-1999 at Boston Children's Hospital, Boston, MA. She worked as research fellow at Boston Children's Hospital, Division of General Pediatrics through NIMH ICORTHA Fogarty International Mental Health and Developmental Disabilities Research Training Program in 2003. She spent her sabbatical year at the Miami Children's Hospital Brain Institute Comprehensive Epilepsy Program in the academic year 2011-2012.
Dr. Yalnizoglu has been working at Hacettepe University Children's Hospital Department of Pediatric Neurology since 1999 as a staff member and she worked as the head of Department of Pediatric Neurology between 2013-2016.

Her primary area of clinical work and research are focused on complex epilepsies and epilepsy surgery in children. Additionally, her recent work extended to rare and undiagnosed neurometabolic/neurogenetic disorders.
Administratively, she served as an elected Board Member of the Turkish Child Neurology Society between 2012-2018. She is member of Turkish National Pediatrics Society, Turkish Epilepsy Society, Turkish Clinical Neurophysiology EEG-EMG Society-Ankara Branch, AOCNA, EPNS, ICNA and AES. She currently serves as a member of the EPNS Committee of National Advisors Training Advisory Board.

L-25

DIAGNOSIS AND TREATMENT FOR NEONATAL SEIZURES IN MALAYSIA

Sangita D. TERUMALAY

Department of Pediatrics, Pediatric Institute, Hospital Kuala Lumpur Malaysia, Malaysia

Neonatal seizures remain a frequent cause of admissions to the neonatal intensive care units in Malaysia. Common causes of seizures are hypoxic ischemic encephalopathy, central nervous system infection and intracranial hemorrhage. Thorough history taking, targeted physical examination coupled with neurophysiological assessment is often required to assess newborns at risk for seizures. When applicable, correlation of seizures with aEEG/EEG is desirable to ensure prompt delivery of antiepileptic drugs. Further characterization to ascertain whether paroxysmal movements are seizures is important to avoid unnecessary and potential side effects of drugs. Phenobarbitone remains the 1st antiepileptic drug of choice is most NICU's in Malaysia.

CURRICULUM VITAE

Academic qualification

NO	QUALIFICATION	AWARDING BODY	YEAR
1.	MBBS University	Malaya (Dean's list)	2002
2.	MRCPCH	Royal College of Paediatrics and Child Health, UK	2007
3.	Subspecialty training (Fellowship in Paediatric Neurology)	Paediatric Neurology Unit, Hospital Pulau Pinang & Hospital Kuala Lumpur	2014
4.	Subspecialty training (Fellowship in neonatal Neurology)	The Hospital for Sick Children Toronto and University of Toronto, Canada	2015

Appointments in Ministry of Health, Malaysia

	DESIGNATION	DATES
1	Houseman August	2002-May 2004
2	Medical officer	June 2004-Sept 2007
3	Clinical specialist and pediatrician	October 2007-Dec 2010
4	Clinical Fellow in pediatric and neonatal neurology	January 2011-Feb 2015
5	Pediatric and Neonatal Neurologist	March 2015 till date

Introduction

Paediatric neurology is an expanding subspecialty in the Ministry of Health Malaysia, offering services primarily to children with neurological and developmental disorders. I started the pediatric neurology subspecialty training under Dato' Dr Hussain Imam, Dr Vigneswari Ganesan and Dr Khoo Teik Beng at Pulau Pinang Hospital and Pediatric Institute, Hospital Kuala Lumpur. Management of newborns with refractory seizures and other neurological issues was identified as an area in pediatric neurology that needed to be developed further. I subsequently trained for one year at the Hospital for Sick Kids Toronto, Canada, a tertiary center with established pediatric neurology training and neonatal neurology programs.

I was attached to the neonatal intensive care unit (NICU) and managed newborns with complex neurological disorders under the tutelage of Dr Steven Miller, Head of the Division of Neurology and a Senior Scientist in Neurosciences & Mental Health at The Hospital for Sick Children. From March 2015, I have been practicing as a pediatrician, pediatric & neonatal neurologist at the Pediatric Institute, Hospital Kuala Lumpur. In addition to pediatric neurology and general pediatric responsibilities, I have taken a lead role in developing the neonatal neurology services in Hospital Kuala Lumpur and Malaysia.

HOW TO PROTECT THE NEONATAL BRAIN

L-26

Alistair J. GUNN

University of Auckland, New Zealand

Acute post-asphyxial encephalopathy occurring around the time of birth remains a major cause of death and disability. The seminal insight that led to active neuroprotective treatment is that even after profound asphyxia (the primary phase), many brain cells show initial recovery from the insult during a short latent phase, typically lasting approximately 6 h, only to die hours to days later after a secondary deterioration characterized by seizures, cytotoxic edema, and progressive failure of cerebral oxidative metabolism. Animal and human studies designed around this conceptual framework have shown that moderate cerebral hypothermia initiated as early as possible but before the onset of secondary deterioration, and continued for a sufficient duration to allow the secondary deterioration to resolve, has been associated with potent, long-lasting neuroprotection. Recent clinical trials show that while therapeutic hypothermia significantly reduces morbidity and mortality, many babies still die or survive with disabilities. The challenge for the future is to find ways of improving the effectiveness of treatment. This presentation will dissect the known mechanisms of hypoxic ischemic brain injury in relation to hypothermic neuroprotection to examine the viability of different strategies of improving neurological outcome after asphyxia.

CURRICULUM VITAE

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE(if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Otago University, New Zealand	MBChB	12/1982	Medicine
Royal Australasian College of Physicians	FRACP	6/1992	Paediatrics
University of Auckland, New Zealand	PhD	5/1993	Paediatrics

A. Personal Statement

My programme of research is in the mechanisms, detection, and treatment of perinatal and prenatal brain injury. I have played a leading role in developing models of injury in the fetal sheep that allow direct translation of preclinical findings to the clinic. I am best known for my preclinical and clinical studies of neuroprotection with head cooling after perinatal asphyxia. We knew that the great majority of acute brain injury in term infants evolved after the time of birth, offering the tantalizing possibility that it might be possible to intervene to improve outcomes. Hypothermia has been proposed for resuscitating infants after perinatal asphyxia for over 300 years, but there was insufficient evidence to underpin clinical testing. My studies used a well-defined large animal model of acute cerebral ischemia to prove for the first time ever that mild cooling initiated well after the end of severe fetal oxygen deprivation can be neuroprotective, to define the optimal depth and duration of cooling and to systematically explore the window of opportunity for improved outcomes. These studies provided the key parameters for subsequent clinical translation. More recently I led a study that further showed that extending the duration of mild hypothermia from 3 to 5 days did not improve neural outcomes.

L-27

UMBILICAL CORD BLOOD STEM CELL THERAPY FOR NEONATAL ENCEPHALOPATHY

Masahiro TSUJI

Kyoto Women's University, Japan

Neonatal encephalopathy refers to acute brain dysfunction that arises during and immediately after the birth, and its incidence is 1-2 per 1000 live births. Neonatal hypoxic-ischemic encephalopathy accounts for almost 80% of the cases and neonatal stroke account for 5-10% of the case. Effectiveness of currently available treatments for neonatal encephalopathy is limited, and neonatal encephalopathy frequently results in life-long neurological impairments such as cerebral palsy, mental retardation, and epilespy. Recently, cell-based therapies gather much attention as novel therapies for neonatal encephalopathy.

Umbilical cord blood (UCB) is a rich source of a variety of stem cells such as CD34+ cells (hematopoietic stem/endothelial progenitor cells) and is readily obtainable without invasive procedure. We developed a highly reproducible mouse model of neonatal stroke, i.e., permanent middle cerebral artery occlusion (MCAO). Using this model, we demonstrated that intravenous injection of human UCB CD34+ cells 48 hours after the MCAO significantly ameliorated morphological brain injury and partially ameliorated behavioral deficits. We observed very limited number of infused cells in the brains after UCB CD34+ cell infusion. Hence, we assume that cell replacement is not the mechanism of action. We showed that increased cerebral blood flow and amelioration of changes in metabolites in the brain after the cell infusion are at least part of the mechanisms of the treatment.

Based on this preclinical study, we started a multi-center phase I clinical study, named Autologous cord blood therapy for neonatal encephalopathy (NIH ClinicalTrials.gov: NCT02256618). Just recently, this phase I study was completed without noticeable adverse events.

CURRICULUM VITAE

Professor, Department of Food and Nutrition, Kyoto Women's University
35 Imakumano, Kitahiyoshi-cho, Higashiyama-ku, Kyoto 605-8501 Japan
E-mail: tsujima@kyoto-wu.ac.jp

Professional Experience

2000-2001	Clinical fellow, Department of Pediatrics,Kobe City General Hospital, Hyogo
2002-2004	Post-doctoral research fellow, Department of Neurology, Kennedy Krieger Institute, Johns Hopkins University, U.S.A
2004-2009	Chief physician, Department of Pediatrics, Kobe City General Hospital, Hyogo
2009-2018	Laboratory Chief, Department of Regenerative Medicine and Tissue Engineering, National Cerebral and Cardiovascular Center
2018-present	Current Positions (See above)

Education

1992	M.D. Faculty of Medicine, Tottori University
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Recent Publications

1. Tanaka E, Ogawa Y, Mukai T, Sato Y, Hamazaki T, Nagamura-Inoue T, Harada-Shiba M, Shintaku H, **Tsuji M**. Dose-Dependent effect of intravenous administration of human umbilical cord-derived mesenchymal stem cells in neonatal stroke mice. *Front Neurol* 9:133, 2018
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DEVELOPMENT A NOVEL REGENERATIVE TREATMENT FOR PERINATAL BRAIN INJURY WITH MUSE CELLS

L-28

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Perinatal hypoxia-ischemia (HI) is an important cause of neonatal death and permanent neurological deficits. Stem cell therapy using various cell sources has been recently identified as a novel therapy for perinatal HI. Multilineage-differentiating stress-enduring (Muse) cells are a novel type of endogenous stem cells that are able to self-renew, and display pluripotency. Muse cells injected intravenously migrate into injured sites and spontaneously differentiate into functional cells.

We expected that the Muse cells could exert a treatment effect for perinatal HI and we evaluated the effect with perinatal HI model rats, which was made by ligation of the left carotid artery, followed by a 60-min of hypoxic (8%) exposure. We have shown that 1) Intravenous administration of the Muse cells did not increase mortality or shorten life span. 2) Muse cells, but not non-Muse mesenchymal stem cells (MSCs), migrated into injured brain and differentiated into neurons in perinatal HI model rats. 3) Muse cells injected intravenously ameliorated learning deficit and motor impairment induced by HI in the rat model, and the treatment effect is much more evident than that done by non-Muse MSCs.

In addition, the evaluations performed by the contract research organization with clinical grade Muse cells developed by Life Science Institute, Inc. also indicated that the clinical grade Muse cells had treatment effects without any adverse effects in the neonatal model.

In the following project, we are going to plan an exploratory investigator-initiated clinical trial to reveal the safety and the feasibility of the treatment with the Muse cells.

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Medical Training / Work

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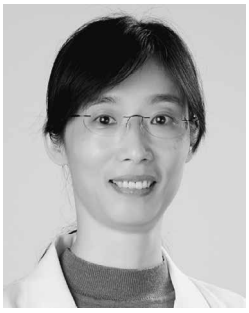
L-29

NEUROLOGICAL OUTCOMES IN INFANTS WITH NEONATAL SEIZURES RELATED TO HYPOXIC-ISCHEMIC ENCEPHALOPATHY



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In neonatal hypoxic-ischemic encephalopathy (HIE), seizures often signal the secondary injury phase and may further aggravate brain damage. Seizures cause local energy depletion, alteration of cerebral blood flow and nutrient supply, and further induce neuronal disintegration and apoptosis after HIE. In pre-hypothermia era, numerous studies have shown a relationship between the presence of clinical and electrographic seizures, especially status epilepticus, and abnormal neurological outcomes including death, dyskinetic or spastic quadriplegic cerebral palsy, epilepsy, and intelligence disabilities. In recent post-hypothermia era, therapeutic hypothermia was noted to decrease overall neuronal excitability and seizure propagation, downregulates cerebral metabolism and inflammation, and nowadays is globally applied in treating moderate and severe HIE. However, it is more effective in moderate than severe HIE, and it reduced total seizure burden significantly in moderate HIE but not severe HIE. Severe HIE is known to be at risk of having more basal ganglia/thalamus and total cortical injury on magnetic resonance imaging examination. Thus, adverse neurological outcomes in infants with neonatal seizures after HIE mainly depended by the HIE stage and seizure burden in neonatal period, irrespective of therapeutic hypothermia.

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Recent Publication

1. Wu PM, Shih HI, Yu WH, Chen LW, Wang LC, Huang CC, **Tu YF**. Corpus callosum and cerebellar vermis size in very preterm infants: Relationship to long-term neurodevelopmental outcome. Pediatr Neonatol. 2018
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ABSTRACTS

Oral Presentation

O-1 TRANSCRANIAL DOPPLER EXAMINATION FOR NEONATES RECEIVING THERAPEUTIC HYPOTHERMIA AND THE SEVERITY OF MRI BRAIN INJURY

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Background:
Middle cerebral artery (MCA) supplies 80% of the cerebral hemisphere. In contrast to the studies on anterior cerebral artery, there was no study investigating the relationship of MCA flow velocity and the severity of brain injury. The aim of this study was to assess the correlation between cerebral blood flows by transcranial Doppler sonography and the severity of magnetic resonance imaging (MRI) brain injury in asphyxiated neonates with HIE who received therapeutic hypothermia.
Methods:
This retrospective cohort study was conducted in the neonatal intensive care unit at Chang Gung Memorial Hospital between April 2011 and May 2014. Neonates with HIE who received therapeutic hypothermia, transcranial Doppler examinations, and brain MRI were eligible. Brain MRI was performed at 1-2 weeks of age. Severity of MRI brain injuries was assessed by the MR scoring system proposed by Barkovich. Serial transcranial Doppler examinations were performed in three distinct phases (pre-hypothermia, hypothermia, and post-hypothermia) in this study.
Results:
Twenty-six neonates were enrolled for analysis. Neonates with abnormal mean cerebral blood flow velocity of MCA in the hypothermia phase had high rate of brain MRI abnormalities and higher MR scores of basal ganglia. However, there were no statistical differences between abnormal mean cerebral blood flow velocity of MCA and brain MRI abnormalities during pre- and post-hypothermia phases.
Conclusion:
During therapeutic hypothermia, mean cerebral blood flow velocity of MCA is associated with the severity of MRI brain injury in neonates with HIE.

O-2 CONTINUOUS ELECTROENCEPHALOGRAPHIC MONITORING IN THE CRITICAL ILLNESS NEWBORN WITH HIGH RISK OF ENCEPHALOPATHY

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Background
Continuous electroencephalographic monitoring was used with increasing frequency in newborn with high risk of encephalopathy to provide insight into brain function and identify electrographic seizures. In our study, we aimed to identify the prevalence of electrographic seizure and correlate the push-button for suspected clinical seizure and electrographic finding in newborn with high risk of encephalopathy.
Methods
We conducted this prospective cohort study in a tertiary paediatric intensive care unit between October 1, 2017 and September 30, 2018. Newborns with high risk of encephalopathy receiving continuous electroencephalographic monitoring were eligible. The clinical data were reviewed.
Results
In this one year preliminary study, a total of 26 critical illness newborn with high risk of encephalopathy underwent electroencephalographic monitoring were enrolled. Electrographic seizures occurred in 8 patients (30.7%), of whom 3 patients (37.5%) had electrographic status epilepticus and 4 patients (50%) had exclusively electrographic-only seizures. Besides, 77 push-buttons for abnormal paroxysmal events (sudden, stereotyped, unexplained clinical events) was noted in 19 patients, of whom 22 (28.6%) push-buttons in 4 patients were clinical-electrographic seizures.
Conclusions
Electrographic seizures occurred in 30.7% of critical illness newborn with high risk of encephalopathy, often constituted electrographic status epilepticus, and were often electrographic-only, thereby requiring electroencephalographic monitoring for identification. Besides, only 28.6% abnormal paroxysmal events (sudden, stereotyped, unexplained clinical events) were clinical-electrographic seizures.
Keyword: continuous electroencephalographic monitoring; critical illness newborn; high risk of encephalopathy

PREVALENCE OF INTERICTAL SCALP EEG HIGH FREQUENCY OSCILLATIONS IN PEDIATRIC EPILEPSY MONITORING UNIT

O-3

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RATIONALE:
High-frequency oscillations (HFOs), including ripples (R:80-250Hz) and fast ripples (FR:250-500Hz), are promising biomarkers of epileptogenesis, yet detectability of scalp EEG HFOs, especially FR, is still debated. We hypothesized interictal scalp HFOs are prevalent among children with epilepsy.
METHODS:
We identified 99 children who underwent Pediatric Epilepsy Monitoring Unit (EMU) admission at UCLA with scalp EEG sampling frequency at 2000 Hz over a 16-month period. Two pediatric electroencephagraphers blinded to clinical information visually marked interictal R and FR in a 1 minute artifact-free sample during non-REM sleep. The identified events were adjudicated by a third electroencephalographer and further validated with time-frequency analysis.
RESULTS:
There were 90 subjects (median age 49 months, range 1 month - 27 years) analyzed for HFOs (9 subjects were excluded due to significant artifacts). Interictal scalp HFOs were found in 24 children, and all had epilepsy except one. The prevalence of HFOs was much higher in children with epilepsy than children without epilepsy (34 vs. 4%, p=0.005). FR were found in 8 children (either established drug-resistant epilepsy, new onset epileptic spasms or focal epilepsy in tuberous sclerosis complex). Children with FR were significantly younger than children with epilepsy without HFOs (median age 12.5 vs. 80.5 months, p=0.02).
CONCLUSIONS:
Scalp EEG HFOs were prevalent among children with epilepsy, and its presence predicts epileptogenicity especially in younger children.

INCREMENT OF GABA NEUROTRANSMISSION IN KCNQ2 GENE MUTATION MODEL OF NEONATAL EPILEPSY

O-4

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Mutations of the KCNQ2 gene, which encodes the Kv7.2 subunit of voltage-gated M-type potassium channels (M-channels), have been associated with epilepsy in the neonatal period. This developmental stage is unique in that the neurotransmitter GABA, which is inhibitory in adults, triggers excitatory action due to a reversed chloride gradient.
To examine whether KCNQ2-related neuronal hyper-excitability involves neonatally excitatory GABA, we examined one-week-old knock-in mice expressing the Kv7.2 variant p.Tyr284Cys (Y284C) (Tomonoh et al., 2014). To make visible GABAergic interneurons in the electrophysiological experiments, all the mice used in this study possessed the VGAT-Venus transgene and these mice specifically expressed Venus fluorescent protein in GABAergic neurons under the control of the mouse vesicular GABA transporter (VGAT) promoter (Wang et al., 2009).
Brain slice electrophysiology revealed elevated GABAergic interneuron activity with respect to presynaptic firing and postsynaptic GABAergic current frequency in the CA1 legion of hippocampus. Blockade with the GABAA receptor antagonist bicuculline decreased ictal bursting in divalent ion-challenged brain slices, which is consistent with GABA mediating an excitatory function that contributes to the hyper-excitability observed in mutant animals.
We conclude that excitatory GABA contributes to the phenotype in these animals, which raises the question of whether this special type of neurotransmission has broader importance in neonatal epilepsy than is currently recognized.

O-5 INFANTILE EPILEPTIC ENCEPHALOPATHIES: EVALUATING IN THREE CASES

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Purpose: Early infantile epileptic encephalopathies (EIEEs) are a group of neurological disorders characterized by early-onset refractory seizures, severe electroencephalographic (EEG) abnormalities, and developmental delay and/or intellectual disability. Here, We presented three patients diagnosed as epileptic encephalopathy with symptoms begining in the first year of life, multiple seizure types and different genetics.

Case Summaries and Results: All patients were female and born from nonconsanguineos Turkish parents. Case1 (C1) was delivered at term after uneventful pregnancy and labor. Her intractabl focal clonic seizures started at the age of 4 months (mo). She controlled with carbamazepine at the age of 10 months (mo). Genetic test revealed a heterozygous mutation in RHOBTB2 gene. Case 2 (C2) had a history of late preterm delivery. She had seizure induced with fever which were started at the age of 12 mo. Intractabl seizures were partially responsive to valproat. She had a heterozygous mutation in STXBP1 gene that is related with IEEE4. Case 3 (C3), who had a first seizure at the age of 2 days, was followed for 3 mo due to resistant seizures such as myoclonic, tonic, generalize tonic clonic at ICU. Multipl antiepileptic drugs and combinations and ketojenic diet were tried but failed to control seizures. She had a heterozygous mutation in KCNQ2 gene.

Conclusion: It is very common that the whole-exome and genome sequencing technologies are applied to use in individuals with early infantile epileptic encephalopathies. Further studies are needed for a better understanding of the phenotype/genotype correlation in EIEEs.

ABSTRACTS

Poster Presentation

P-1

ELECTROPHYSIOLOGICAL PROPERTIES OF EXCITATORY OR INHIBITORY NEURONS DERIVED FROM INDUCED PLURIPOTENT STEM CELLS (IPSC) IN ANGELMAN SYNDROME

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[Purpose]
Angelman syndrome (AS) is a neuro-developmental disorder caused by loss-of-function of the maternally expressed *UBE3A* gene. The main manifestation including developmental delay and epilepsy usually appears after late infancy. While the majority of AS patients suffers from a large deletion of the relevant chromosomal region and shows more typical phenotype, the remaining patients are caused by functional deficits of UBE3A such as uniparental disomy, *UBE3A* mutation and imprinting defect. The pathophysiology of AS is largely unclear partly because only *Ube3a* mutation mice is currently available as model mice of AS. To investigate neuronal dysfunction of AS on each genotype, we analyzed neuro-electrophysiological properties of induced pluripotent stem cell (iPSC)-derived neurons from AS patients.
[Methods]
Conditional expression of the transcription factor, either Neurogenin 2 or Ascl1/Dlx2, exclusively and efficiently induced the generation of glutamatergic or GABAergic neurons from iPSC of AS subject, respectively. One month after induction, we analyzed the properties of each neuron by using patch-clamp recording.
[Results]
Matured intrinsic membrane properties were maintained in each AS genotype. Both excitatory and inhibitory neurons from AS patients, in particular, the deletion patients showed more efficient firing properties than control subjects.
[Conclusions]
With efficient systems for neuronal differentiation, our result was opposite to the previous AS-iPSC research using a conventional protocol, suggesting that time-course of neuronal maturation was altered in AS. Efficient firing in AS may suggest imbalance between phasic and tonic inhibitory systems. These results may provide a clue for understanding the mechanisms of AS.

P-2

ASSOCIATION BETWEEN BRUSH OCCURENCE ON ELECTROENCEPHALOGRAM AND NEURODEVELOPMENTAL OUTCOME IN PREMATURE INFANTS

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Background: Subplate neurons (SPN) are transiently expressed group of neurons that have important roles in cortical development and corticocortical connections. Recent animal and human studies have suggested that brush (delta brush) seen in the preterm electroencephalogram (EEG) is thought to reflect SPN activity. We hypothesize that SPN injury is associated with abnormal neurodevelopment in premature infants and clarify whether brush occurrences in the preterm EEG predict later neurodevelopmental outcome. Method: EEG from 36 extremely low birth weight infants without severe brain injuries admitted to our neonatal intensive care unit from 2012 to 2017 were analyzed. Conventional 8ch EEG were recorded at 30, 32, and 36 weeks postmenstrual age (PMA). Brush was defined as a rhythmic fast wave with frequency of 8-20 Hz, amplitude 20-40 microV, lasting more than 0.4 seconds. The brush occurrence (/min) was calculated as a sum from 8ch EEG, separated by continuous and discontinuous EEG pattern. Developmental quotient (DQ) was assessed at a corrected age of 18 months. Result: Brush occurrences at 30, 32, and 36 weeks PMA were 16.4, 20.4, and 22.5/min, respectively, in continuous pattern and 7.5, 9.4, and 1.9/min, respectively in discontinuous pattern. Brush occurrences at 36 weeks PMA only correlated negatively with DQ in continuous ($P = 0.03$) and discontinuous ($P = 0.02$) patterns. Brush occurrences were not associated with dysmature pattern on EEG. Conclusion: The negative correlation between brush occurrences at 36 weeks and 18months DQ could indicate the delay of spontaneous regression of SPN in extremely low birth weight infants.

P-3

CLINICAL FEATURES AND ELECTROCLINICAL EVOLUTION OF 22 PATIENTS WITH EPILEPTIC SPASMS WITHOUT HYPSARRHYTHMIA

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Purpose: Epileptic spasms without hypsarrhythmia ; ESwoH is a condition which shows ES, but its electroencephalogram is not typical hypsarrhythmia. This study aimed to examine whether there was a difference in an effect of treatment or ACTH therapy, seizure outcome and evolutions of electroclinical features by initial EEG patterns. Methods: According to the pattern of background activities, we divided 2 groups: group1, background activities were normal or limited to localized intermittent slow waves; group2, intermittent slow waves appeared on 2 or more lobes or generalized. The subjects were 22 children, group1 N=10, group2 N=12, who diagnosed ESwoH and received therapies in Saitama children's medical center from 2007 to 2017. Results: age at onset of ES, 6 months of age, median ; follow up periods, 44 months, median ; preceding other seizure, group1 5 out of 10, group2 4 out of 12; response to ACTH, group1 0 out of 10, group2 1 out of 12. In both groups, epilepsy outcomes were very good, mostly seizure free, when primary therapies were effective. Conversely, in the case of the primary therapies could not work, the outcomes were worse, mostly daily seizure and EEGs developed hypsarrhythmia in 5 out of 7 patients of group2. Conclusions: ACTH might be not effective for the patients of ESwoH. EEG could be likely to develop hypsarrhythmia in future if ES was refractory to the treatment especially in the patients who showed diffuse slow waves in their initial EEGs.

P-4

EEG-FMRI ANALYSIS OF HYPSARRHYTHMIA IN WEST SYNDROME OF UNKNOWN ETIOLOGY

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Objectives: West syndrome is an epileptic encephalopathy characterized by epileptic spasms, hypsarrhythmia on electroencephalogram (EEG) and developmental regression. The pathogenesis of hypsarrhythmia has not been fully clarified. The aim of this study was to explore the neural network of hypsarrhythmia, using simultaneous recordings of EEG and functional MRI (EEG-fMRI).
Methods: We examined 4 patients with West syndrome of unknown etiology by EEG-fMRI at 3T. EEG-fMRI was performed 4 to 16 days after the onset of epileptic spasms before ACTH therapy. The EEG records were reviewed to confirm the timing of periodic hypsarrhythmia during sleep, which were used as events. The temporal information of periodic hypsarrhythmia was used to perform event-related analysis for detecting hypsarrhythmia-related blood oxygenation level-dependent (BOLD) changes ($p<0.05$ corrected for multiple comparison using a family-wise error).
Results: Positive BOLD changes involved multifocal cortices, thalami, hippocampi, and brainstem in all patients and basal ganglia in 3 patients. The maximum t-values were found in brainstem in 2 patients, in frontal lobe in 1 patient, and in occipital lobe in 1 patient. Negative BOLD changes were not observed in any regions.
Conclusion: Our results suggest that abnormal neural network underlying hypsarrhythmia involves the brainstem, which may play a leading role in the abnormal neural network between cortex and subcortical structures in West syndrome. EEG-fMRI is a useful tool for clarifying the pathophysiology of West syndrome.

P-5

CLINICO-ELECTROENCEPHALOGRAPHIC STUDY OF REPETITIVE SLEEP STARTS IN CHILDREN

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[Objective] Repetitive sleep starts (RSS) are clusters of non-epileptic, spasm-like movements occurring during sleep onset. However, their characteristics have yet to be defined. We conducted a clinico-electroencephalographic study of children with RSS to clarify their detailed characteristics. [Methods] A total of 10 children with involuntary movements, "crescendo-decrescendo" muscle activities, and the following characteristics were included: 1) brief muscle contractions or movements involving limbs and trunk simultaneously; 2) repetitive occurrence (i.e., five or more); 3) manifestation during sleep-wake transition and/or sleep stage N1-N2, and 4) absence of ictal electroencephalogram (EEG) changes. Their clinical information and ictal video-EEG data were analyzed retrospectively. [Results] Perinatal hypoxic-ischemic encephalopathy (n = 4), West syndrome of unknown etiology (n = 2) and traumatic brain injury (n = 1) were the background conditions observed at

onset, whereas three children did not present obvious neurodevelopmental disorders at onset. The RSS onset ranged from 3 to 46 months of age. The number of starts in a given RSS cluster, the interval between starts, and the duration of electromyogram activity were between 5 and 547, <1 and 60 seconds, and 0.3 and 5.4 seconds, respectively. None of these parameters differed between children with and without corticospinal tract injury. RSS disappeared spontaneously in five children, and seven did not develop epilepsy. [Conclusion] This is the largest case series of RSS clarifying their clinico-electroencephalographic characteristics. To avoid unnecessary anti-epileptic therapies, clinicians should be aware of this condition and distinguish it from other disorders that exhibit involuntary movements or seizures, especially epileptic spasms.

P-6

ASSOCIATION OF GRAY MATTER VOLUME IN PRETERM INFANTS WITH NEURODEVELOPMENTAL OUTCOMES

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Background: Preterm birth affects brain development and growth and is associated with later neurodevelopmental outcomes. This study aimed to clarify our hypothesis that premature infants are more likely to have lower gray matter volume at term equivalent age, particularly in the temporal lobes, which is in turn associated with adverse neurodevelopmental outcomes, especially in language.

Methods: We evaluated 111 preterm infants of gestational age ≥34 weeks who underwent volumetric MRI at term equivalent age. We excluded infants with periventricular leukomalacia, periventricular hemorrhagic infarction, and twin to twin transfusion syndrome (TTTS). Voxel-based morphometry (VBM) was used to analyze grey matter volume which includes cortical and deep grey matter, and hippocampal volume. Developmental quotient (DQ) assessed at 18 months of corrected age.

Results: Of the 111 infants, data of 82 with sufficient quality of segmentation were studied. The mean (standard deviation) gestational age at birth and at MRI scan were 29.8 (2.6) and 39.3 (2.4) weeks, respectively. The mean (standard deviation) DQ was 88.0 (15.3). VBM analysis revealed that gestational age at birth was positively correlated with widespread gray matter volume, especially in the bilateral temporal lobes, orbitofrontal areas, and deep gray matter (Figure 1). However, none of these areas was correlated with DQ at 18 months of corrected age. Only hippocampus volume at term equivalent age was positively correlated with DQ (Figure 2), although it was not with language domain.

Conclusion: Normal development of the hippocampus is an important predictor of early neurodevelopmental outcome in preterm infant.

P-7

GLYCINE MEASUREMENT USING SHORT AND LONG ECHO TIME PROTON MAGNETIC RESONANCE SPECTROSCOPY IN A NEONATE WITH NONKETOTIC HYPERGLYCINEMIA

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Introduction: In nonketotic hyperglycinemia (NKH), 1H-MRS shows a striking increase in brain glycine levels. However, the signal overlap of glycine with myo-inositol makes it difficult to quantify each metabolite separately. Our aim was to investigate glycine measurement with 1H-MRS using different echo times (TE) in a neonate with NKH.

Methods: Serial single-voxel 1H-MRS in the centrum semiovale was performed with TE of 30 and 270ms in a neonate with NKH on 6, 19, 44 days of age, and the peak area ratios of glycine plus myo-inositol to creatine (Gly+mIns)/Cr was evaluated. Glycine levels of plasma and cerebral spinal fluid (CSF) were also measured on 5, 19, and 44 days of ages.

Results: In both TEs, (Gly+mIns)/Cr showed higher values at first, then decreased subsequently; TE 30msec: 1.43, 1.19, and 1.11, TE 270 msec: 1.05, 0.55, and 0.49, respectively. Both glycine levels of plasma and CSF showed similar decreasing: plasma: 1803.9, 353.0, and 140.0 μmol/L, CSF: 321.6, 135.3, and 69.7 μmol/L, respectively. On 6 days, the patient was comatose, and had no spontaneous respiration. On 19 days, he was lethargic but had spontaneous respirations. On 44 days, his consciousness was almost clear.

Conclusion: The continuing reduction of (Gly+mIns)/Cr with long-TE corresponded more reliably with glycine levels of plasma and CSF than the change with short-TE. In addition to T2 relaxation time effect, myo-inositol also has J-coupling induced-dephasing effect, which results in small signal in long TE. Therefore myo-inositol signal may have a relatively less contribution to (Gly+mIns) in TE 270ms.

P-8

123I-IOMAZENIL SPECT FINDINGS IN CRYPTOGENIC WEST SYNDROME

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[Objective] 123I-iomazenil (IMZ) is a radioactive ligand specific to central benzodiazepine receptors (BZR), which

form a complex with post-synaptic GABA-A receptors. We capitalized on this property to use retrospective statistical image processing to elucidate the pathophysiology of cryptogenic West syndrome. [Method] We selected as subjects 14 patients with cryptogenic West syndrome that showed no abnormal MRI findings, no neurological abnormalities except epileptic spasms, and were not on benzodiazepines. After scanning subjects with a triple-head gamma camera following ligand injection, we used a semiquantitative analytical method consisting of brain surface extraction and anatomical normalization. Radio isotope counts in each region of interest (ROI) were analyzed using our reports methodology as a reference (Pediatr Neurol. 2018). [Result] A total of 9 out of 14 patients were scanned both before and after effective treatments. The first or second line treatment (pyridoxal, ACTH treatment, vigabatrin) was effective in 12 out of 14 cases. Two patients cases were intractable, with both first and second line treatments being ineffective. Pyridoxal was effective in 2 cases, which were scanned following seizure cessation. One case in which pyridoxal was effective presented with relatively high BZR binding despite their age. In comparing before and after effective treatment, 6 out of 9 (67%) cases showed decreased BZR binding in all ROIs after effective treatment. [Conclusion] BZR binding was decreased after effective treatment in cryptogenic West syndrome, a finding which may indicate that effective treatment promotes brain maturation.

P-9

DOES HYPSARRYTHMIA AFFECT RCBF IN THE PATIENTS WITH EPILEPTIC SPASMS?

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Objective: To show effect of hypsarrhythmia to brain function, we compared regional cerebral blood flow (rCBF) between patients with West syndrome (WS) and patients with epileptic spasms (ES) without hypsarrhythmia (ESwoH).
Method: We retrospectively analyzed quantitative values of rCBF in patients with ES under 2 years old. They received treatments at Saitama Children's Medical Center from 2002 to 2017 and met according to the following criteria: 1) normal MRI; 2) ES confirmed by ictal-EEG; and 3) ^{123}I-IMP SPECT was performed before ACTH therapy, and excluded patients with developmental delay and other seizures before the onset in WS. We examined age of onset, days from the onset to the day when EEG was performed, age at the day when SPECT was performed, and rCBF in both groups.
Results: WS and ESwoH included 28 and 8 patients, respectively. There were not significant differences on average age of onset (5.5 vs. 4.8 months) and average age at the day when SPECT was performed (7.7 vs. 7.1 months) between two groups. An average day from the onset to the day when EEG was performed was longer in WS than in ESwoH (27 vs. 14 days, $p<0.05$). None of cortical rCBFs did exhibit significant difference between two groups. Only thalamic rCBF was significantly lower in ESwoH than in WS ($p<0.05$).
Conclusions: rCBF study revealed the difference in thalamus between the patients with hypsarrhythmia and without hypsarrhythmia. We suggested that thalamus played an important role to express hypsarrhythmia.

P-10

DE NOVO PHACTR1 MUTATIONS IN WEST SYNDROME AND THEIR PATHOPHYSIOLOGICAL EFFECTS

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Trio-based whole exome sequencing identified two de novo heterozygous missense mutations [c.1449T>C/p.(Leu500Pro) and c.1436A>T/p.(Asn479Ile)] in PHACTR1, encoding a molecule critical for the regulation of protein phosphatase 1 (PP1) and the actin cytoskeleton, in unrelated Japanese individuals with West syndrome (infantile spasms with intellectual disability (ID)). We then examined the role of Phactr1 in the development of mouse cerebral cortex and the pathophysiological significance of these two mutations and others [c.1561C>T/p.(Arg521Cys) and c.1553T>A/p.(Ile518Asn)], which had been reported in undiagnosed ID patients. Immunoprecipitation analyses revealed that actin-binding activity of Phactr1 was impaired by the p.Leu500Pro, p.Asn479Ile and p.Ile518Asn mutations while the p.Arg521Cys mutation exhibited impaired binding to PP1. Acute knockdown of mouse Phactr1 using in utero electroporation caused defects in cortical neuron migration during corticogenesis, which were rescued by an RNAi-resistant Phactr1 but not by the four mutants. Experiments using knockdown combined with expression mutants, aimed to mimic the effects of the heterozygous mutations under conditions of haploinsufficiency, suggested a dominant negative effect of the mutant allele. As for dendritic development in vivo, only the p.Arg521Cys mutant was determined to have dominant negative effects, because the three other mutants appeared to be degradated with these experimental conditions.

Electrophysiological analyses revealed abnormal synaptic properties in Phactr1-deficient excitatory cortical neurons. Our data show that the PHACTR1 mutations may cause morphological and functional defects in cortical neurons during brain development, which is likely to be related to the pathophysiology of West syndrome and other neurodevelopmental disorders.

P-11

GENETIC HETEROGENEITY IN MYOCLONIC ASTATIC EPILEPSY OR DOOSE SYNDROME

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Myoclonic astatic epilepsy (MAE, Doose syndrome) develops at 2-5 years of age and is characterized by tonic-clonic, myoclonic astatic, and atypical absence seizures with a characteristic theta rhythm in the electroencephalogram (EEG). *SLC2A1*, *SCN1A*, *SLC6A1*, *CHD2*, and *CACNA1H* were reported to be the causative genes for MAE. To further elucidate the genetic background of MAE, blood samples and clinical information including EEG findings were collected from 21 patients with MAE and their parents after informed consent was obtained in written form. Whole exome sequencing was performed for all MAE cases. The male-to-female ratio of the 21 patients was 16:5. All the patients had developed their first seizure between 5 months and 5 years of age. Eleven patients had tonic seizures, four tonic-clonic seizures, and seven other seizure types. Astatic, myoclonic, and atypical absence seizures occurred during the course of their disease. Only four patients were seizure-free. Among the patients with persistent seizures, 4 had motor dysfunction, 14 had intellectual disability (borderline in 4 cases, mild in 9, and severe in 1), and 11 had attention deficit hyperactivity disorder. A missense mutation in *SCN1A* was identified in a patient with features of both MAE and Dravet syndrome, and a novel *de novo* mutation in *SLC6A1* was identified in a patient with typical MAE. The prevalence rate of genetic variants in our cohort of MAE were similar to those previously reported. Thus, the etiology of MAE is considered to be heterogeneous.

P-12

DIFFERENT PHENOTYPES IN THREE PATIENTS WITH *SCN2A* VARIANT

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SCN2A gene heterozygous missense mutations were investigated in three patients with different clinical courses.

(Case presentation) Case 1 (4-year-old male): Apnea attack occurred after birth. Stroke seizures with right ocular deviation, left lower limb flexion and right lower limb extension appeared at 3 days old. Rhythmic sharp-and-spike waves in the left frontal and temporal lobes were noted on an electroencephalogram (EEG), for which treatment with PB and MDL was started at 4 days old. The *SCN2A* mutation c.4718T>C(p.L1573P) was confirmed by genetic testing. VPA and diazepam were ineffective, but lidocaine provided sufficient control. Eventually, the seizures disappeared without medication. The neurological prognosis was good. Case 2 (2-year-old male): Respiratory disturbance developed after birth, with systemic tonic seizures occurring at 8 days old. An EEG revealed high-voltage slow waves. The *SCN2A* mutation c.4780T>C(p.Trp1594Arg) was confirmed by genetic testing. The symptoms were controlled with CBZ, CZP, ZNS and LID, although severe developmental delay persisted. Case 3 (8-month-old girl): Systemic tonic seizures occurred at 1 day old and spasm developed. An EEG revealed a suppression-burst pattern and the patient was diagnosed with Ohtahara syndrome at 3 months old. The *SCN2A* mutation c.4782G>C(p.Trp1594Cys) was confirmed by genetic testing. The symptoms were controlled with PB and mexiletine, although severe developmental delay persisted.

(Conclusion) These patients exhibited close mutation sites, although their neurological prognoses were significantly different. As hypoxic ischemic encephalopathy and Ohtahara syndrome were noted in Cases 2 and 3, respectively, other neurological complications need to be explored with reference to previous reports.

P-13

DISSECTING THE PHENOTYPIC AND GENETIC SPECTRUM OF EARLY CHILDHOOD-ONSET GENERALIZED EPILEPSIES

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Purpose: Although the genetic and clinical aspects of epilepsy with myoclonic-atonic seizures (MAE) and early onset absence epilepsy (EOAE) have been investigated thoroughly, other early childhood-onset generalized epilepsies cannot be classified as specific epilepsy syndromes. In this study, we aimed to delineate the genetic and phenotypic spectrum of early childhood-onset generalized epilepsies, including MAE and EOAE.
Methods: We recruited 61 patients diagnosed with MAE, EOAE, and unclassified generalized epilepsies that shared seizure onset age and types of generalized seizures. Genetic causes were investigated through targeted gene panel testing, whole exome sequencing, chromosomal microarray, and single-gene Sanger sequencing.
Results: Twelve patients were classified as having MAE, 21 as having EOAE, and 28 were unclassified. The clinical features were comparable across groups. Nevertheless, patients with EOAE tended to show better developmental and seizure outcomes. A total of 23 pathogenic sequences and copy number variants from 12 genes were identified (23/61, 37.7%). Genetic etiologies were confirmed in 33.3% (4/12) of the MAE group, 47.6% (10/21) of the EOAE group, and 32.1% (9/28) of the unclassified group. The most frequently identified genes with pathogenic variants were SLC6A1 (6 patients), SLC2A1 (4 patients), and SYNGAP1 (4 patients). Pathogenic variants in SLC2A1 and SLC6A1 were distributed among all 3 groups.
Conclusion: MAE, EOAE, and unclassified early childhood-onset generalized epilepsy patients appeared to be characterized by an overlapping genetic and phenotypic spectrum. SLC6A1 and SLC2A1 appeared to be important genetic causes because pathogenic variants in these genes were identified in all 3 groups.

P-14

THE PREDICTIVE FACTORS FOR LATER DEVELOPMENT OF EPILEPSY IN INFANTS WITH VERY LOW BIRTH WEIGHT

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Purpose: As a result of development of perinatal intensive care, the life and neurodevelopmental prognosis of very low-birthweight (VLBW) infants (birth weight < 1,500 g) has become favorable. However, the nature of the relationship between the risk factors for later development of epilepsy, one of the major neurologic sequelae in VLBW infants, and clinical characteristics remains unclear. The aim of this study is to clarify the incidence and predictive factors for development of epilepsy in VLBW infants.
Methods: All VLBW infants born in Yamanashi prefecture between January 2012 and December 2017 were enrolled. To clarify the predictive factors for later development of epilepsy, we analyzed the relationship between occurrence of epilepsy and clinical characteristics retrospectively.
Results: A total of 271 infants were enrolled in this study (mean gestational age: 28.9 +/- 3.0 weeks, mean birth weight: 1,077 +/- 309 g). Of 271 subjects, 6 (2.2%) experienced unprovoked seizures. All of these 6 patients were diagnosed with symptomatic focal epilepsy. Patients with congenital neurological anomaly and presence of neonatal seizure had a significantly higher risk of developing epilepsy ($p < 0.05$ and $p < 0.05$, respectively). With the exception of congenital neurological anomaly, 3 (1.1%) of 264 VLBW infants developed epilepsy. In this group, patients with both chorioamnionitis (CAM) and being small for gestational age (SGA) had a significantly higher risk of developing epilepsy ($p < 0.05$).
Conclusion: These findings suggest that VLBW infants with SGA presenting with CAM may be at risk for the development of epilepsy later in life.

P-15

RASMUSSEN SYNDROME: ASSESSMENT OF CLINICAL FEATURES IN PATIENTS WITH DIFFERENT INTELLECTUAL LEVELS

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Background: Rasmussen syndrome (RS) manifest deterioration in the intellectual ability, but the clinical course can vary.
Objective: To assess the differences of the clinical features between the individuals with better and worse intellectual ability in RS.
Subjects and Methods: The medical records of patients with RS visiting National Center of Neurology and Psychiatry between year 2001 to 2018 were retrospectively reviewed. The clinical and imaging features as well as Intelligence Quotient(IQ)/Developmental Quotient(DQ) were assessed.

Result: A total of 7 patients (2 male, 5 female) were identified to be eligible to the study. The mean age of last follow up was 15.7 years (SD 9.2). There were 3 patients with IQ/DQ ≥70, and 4 with IQ/DQ <70 at the last follow-up. The comparison of IQ/DQ ≥70 vs <70 group showed: the average onset age 9.3 (SD 5.1) vs 5.5 (SD 5.4) years, average time to the first immunotherapy 4.5 (SD 5.5) vs 2.1 (SD 1.3) years, brain atrophy within one year after the onset 0 vs 75 %, performance of brain surgery 66 vs 25%.
Conclusion: Patients with better intellectual prognosis had later onset age and negative sign of brain atrophy in the first year in our cohort; longer time before the immunotherapy initiation and the lower rate of undergoing surgery could have been due to a more benign nature of the disease. Further study is needed, but our preliminary data may include a potential predictor of intellectual ability in RS.

P-16

EFFECTIVENESS OF ACTH THERAPY FOR INFANTILE SPASMS WITH A NOVEL *TUBB2A* MUTATION; A CASE REPORT

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Background The *TUBB2A* gene has recently been reported to be associated with brain malformation. Patients with *TUBB2A* mutations often show refractory epilepsy. Infantile spasms are also observed in patients with *TUBB2A* mutations; however the effectiveness of adrenocorticotropic hormone (ACTH) therapy in such patients has not been reported.
Case The patient was a 7-month-old boy. He was the second child of nonconsanguineous parents, and he had a healthy older sister. Lateral ventricular enlargement was detected at 32 weeks of gestation. He was born at 41 weeks of gestational age, without complications. He showed microcephaly (head circumference: -2.8 SD). Brain magnetic resonance imaging (MRI) revealed dysmorphic basal ganglia. This finding suggested tubulinopathy. We performed whole exome sequencing to investigate the genetic cause of tubulinopathy, and identified a *de novo* mutation in *TUBB2A* (c.736C>G, p.Leu246Val). He had severe development delay and suffered from infantile spasms at 6 months of age. Typical hypsarrhythmia was not recognized on electroencephalography (EEG); however, multifocal spike waves were frequently observed. Valproic acid was ineffective. After 2 weeks of daily injection of synthetic ACTH (0.0125 mg/kg), and one week of injections every other day, the patient's seizures ceased. Epileptic discharge was not detected on EEG. As a side effect, brain atrophy appeared on brain MRI, and mild myocardial hypertrophy was observed on echocardiography.
Conclusion Topiramate has previously been mentioned as an effective treatment for epilepsy caused by the *TUBB2A* mutation. However ACTH therapy may also be an effective treatment.

P-17

PERAMPANEL AS EFFECTIVE ADD-ON ANTIEPILEPTIC DRUG FOR REFRACTORY EPILEPSY IN A PATIENT WITH MECP2 DUPLICATION SYNDROME

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Background:
The MECP2 gene was reported associated with maturation of the central nervous system and in forming synaptic contacts. Patients with MECP2 duplication syndrome(MDS) may present with infantile hypotonia, mental retardation, developmental delay, recurrent infections, progressive spasticity and epilepsy. Approximately half of all these patients develop refractory epilepsies. In previous studies, most of the patients had slowing of background in EEG and some had epileptic waves. Moreover, there was no previous report about the efficacy of Perampanel in refractory epilepsy of patient with MDS.

Case report:
In this report, we describe a case of MECP2 duplication syndrome(DOI: 10.1016/j.gene.2013.10.001) in a 15-year-old boy who presented dysmorphic features, developmental delay, progressive spasticity and recurrent infection. The patient had first seizure onset at 13 months old and developed into refractory epilepsy at 7 years old. The frequent atypical absence and occasional tonic seizures were refractory to multiple antiepileptic medications. During the long-term follow up, EEG revealed slowing of background and progression of pathological findings. Image study showed cerebral atrophy. As frequent absence seizure persisted with three antiepileptic drugs, Perampanel was added and the frequency of absence and versive seizure decreased dramatically from five times a day to once in 2-3 days.

Conclusions:
Our report demonstrate long-term progression of electroencephalographic abnormalities in patient with MDS. The clinical improvement of seizures indicate that Perampanel may be an option as add-on therapy for medically refractory focal seizures in patient with MECP2 duplication syndrome.

KEYWORDS: MECP2, MECP2 duplication syndrome,

Perampanel.

P-18

THERAPEUTIC EFFECTIVENESS OF PHENYTOIN IN EPILEPSY OF INFANCY WITH MIGRATING FOCAL SEIZURES CAUSED BY MOSAIC *SCN2A* MUTATION: AN INFANTILE CASE REPORT

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Introduction: *SCN2A* encodes the neuronal voltage-gated sodium channel $Na_v1.2$. Mutations in *SCN2A* lead to various epilepsies, epileptic encephalopathies, or neurodevelopmental disorders. Here we report a case of epilepsy of infancy with migrating focal seizures (EIMFS) caused by one missense mutation in *SCN2A* with mosaicism. We further speculate about the therapeutic mechanisms of phenytoin (PHT).

Case report: A full-term male infant without any perinatal abnormalities developed epileptic episodes, including apnea, ocular deviation, and brief tonic seizures, beginning on his second day of life. His physical examination and laboratory findings were normal, except for left cerebral hemispheric atrophy on brain MRI. Electroencephalogram during an ictal phase indicated EIMFS because seizure activity arose independently in both hemispheres and migrated from one to the other. After that, he was diagnosed with intractable epilepsy, EIMFS, and severe psychomotor developmental delays. Surprisingly, PHT was the only effective anti-epileptic drug (AED) for his seizures, and many AEDs including PB, CBZ, ZNS, LEV, CLB, and KBr were ineffective. Whole exome sequencing analysis for genetic diagnosis of epileptic encephalopathy revealed one *de novo* missense mutation of the sodium channel gene, *SCN2A* (c.488C>T, p.Thr163Ile), with a 15.4% mosaicism.

Discussion: In our case of EIMFS, the therapeutic effects of PHT suggest that the mutation c.488C>T of *SCN2A* might cause a gain-of-function effect on the sodium channel. Our results also indicated that a genetic diagnosis of infantile epileptic encephalopathy might enable patients to receive personalized medicine.

P-19

EFFICACY OF VITAMIN B6 IN EPILEPSY WITH KCNQ2 MUTATION

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Background: Mutations in the KCNQ2 gene, encoding for a subunit of potassium channels, are known to cause early infantile epileptic encephalopathy-7 (EIEE7) and benign familial neonatal seizures-1 (BFNS1). EIEE7 is characterized by drug-resistant seizures. Recently, several reports suggested that epilepsy with KCNQ2 mutations may respond to vitamin B6 therapy. We report here an infant with KCNQ2 encephalopathy with vitamin B6-responsive epilepsy.Case: The patient was a 3-year-11 month old boy. He was born at 38+2 weeks with a birth weight of 2908g and Apgar score of 6/8. He showed drowsiness, hypotonia and poor feeding. Subtle tonic seizures started at 2 days of age, and became remarkable at 14 days. He was admitted to our PICU. Metabolic screening and brain MRI were negative. Asymmetrical clonic jerks and myoclonias were noted. Interictal EEG showed a multifocal spike-wave complexes and slow waves. Treatment with phenobarbital and midazolam was ineffective, but that with vitamin B6 gradually reduced seizure frequency with cessation at age 12 weeks. Nevertheless, he had profound mental retardation, axial hypotonia and mild dystonic quadriplegia. Whole-exome sequencing revealed a c.740C>T mutation of KCNQ2. Conclusion: Vitamin B6 therapy may be effective in epilepsy with KCNQ2 mutations.

P-20

HOSPITAL-BASED ANTIEPILEPTIC DRUG UTILIZATION STUDY IN JAPANESE PATIENTS WITH CHILDHOOD-ONSET EPILEPSY

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<Purpose> Over ten years behind the U.S.A. and European countries, nine new antiepileptic drugs (AEDs) have been approved since 2006 in Japan. This study aims to determine the trends in AED use in our children's hospital

<Methods> We searched our hospital database for all records of AED regimens between 2004 and 2017. Regardless of dose and duration, administration of a specific AED to one person was defined as one prescription. In each year, the prescription rate (%) was calculated by dividing the number of prescriptions of a specific AED by total number of prescriptions. In this study, new AEDs includes GBP, TPM, LTG, LEV, STL,

RFN, VGB, PER, and LCM in marketing-date order. Other AEDs, including ZNS (available in 1989), were classified as conventional AEDs.
<Results> Between 2004 and 2017, the annual number of patients receiving AED ranged from 1,074 to 1,622. Before 2006, CBZ was the most frequently prescribed AED (prescription rate 24%), followed by BZPs (22%) and VPA (19%). Although VPA remained the mainstay of epilepsy treatment, the prescription rates of CBZ and BZPs showed declining trend after 2007. Alternatively, the annual prevalence of new AEDs use increased from 5% in 2007 to 24% in 2017. Of note, LEV prescription rate remarkably increased. In 2017, the prescription rates were shown as follows: VPA (27%), LEV (14%), CBZ (14%), BZPs (13%), PB (7%), ZNS (6%), LTG (4%), and TPM (3%).
<Conclusion> After introduction of new AEDs to market, therapeutic options for treatment of childhood-onset epilepsy increased in Japan.

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AN EFFECTIVENESS OF TRICLOFOS SODIUM ON OHTAHARA SYNDROME WITH A SUBTYPE OF PONTOCEREBELLAR HYPOPLASIA; A CASE REPORT

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We illustrate a case report of Ohtahara syndrome found in a 4¯month¯old infant, whose epileptic spasms and partial tonic seizures were markedly improved after the administration of triclofos sodium. She was a product of 38 weeks´ gestation, delivered virginally, weighing 2,242g at birth. Severe tachypnea and vomiting were noted 10 hours after birth. Laboratory studies showed hypoglycemia and severe lactic acidosis. Because frequent seizure developed on the 9th day after birth, she was transferred to our hospital. Neurological examination showed hypotonia and muscle weakness. MRI exhibited markedly atrophic changes in cerebrum, cerebellum and pons. Genetic study on this patient showed homozygous mutation was identified in mitochondrial arginyl¯tRNA synthetase 2 (RARS2) gene, namely c.944G>C (p.R315P). Interictal EEG showed suppression¯burst pattern (SBP) with generally low voltage background activities. On video EEG, spasms with short tonic limbs and head movement or with twitching of lower limbs are associated with ictal high¯voltage slow wave discharge, which were frequently followed by severely attenuated activities. Partial seizures with left tonic movements and versine head turning movements to the right side were seen with ictal focal rhythmic theta wave discharge in the right hemisphere. These seizures are not responded to the intravenous administration of midazolam, levetiracetam, pyridoxal phosphate, fosphenytoin, and phenobarbital. Conventional antiepileptic drugs including NZP, ZNS, and LCM were ineffective to the seizures, did not improved SBP. However, administration of triclofos sodium improved seizure and SBP. We suggest that triclofos sodium may be one of optional choice for the treatment of Ohtahara syndrome.

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SUCCESSFUL TREATMENT WITH PERAMPANEL TO CONTROL MYOCLONIC SEIZURE IN AN INFANT WITH NEURONAL CEROID LIPOFUSCINOSIS TYPE 14

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Neuronal ceroid lipofuscinosis (NCL) is a type of progressive myoclonic epilepsy (PME), which is hard to be controlled by various antiepileptic drugs. We present a case of young male child with severe developmental deterioration and refractory epilepsy who was diagnosed with PME and followed. He had no family history except that his elder brother had PME and had died at nine years old. The present child had no abnormal events during his perinatal period and normal development until almost 6 months old; however, he was referred to our hospital because of developmental delay at the age of 10 months. Since 12 months old, he has had myoclonic seizures. By two years of age, his development had rapidly deteriorated and he had become bedridden. Using next-generation gene analysis of his lymphocytes, we identified the presence of a homozygous variant of *KTCD7*. The missense variant was reported as pathogenic and is a known cause of CLN14. Although his myoclonic seizures were not controlled by either levetiracetam or clonazepam, adding perampanel (PER) has proven effective in nearly controlling his seizures. PER is a newer antiepileptic drug that acts as an AMPA receptor agonist in the brain and can be used to control both generalized and focal seizures. There are some reports that PER is also effective for other types of PME such as Lafora disease, Unverricht-Lundborg disease, and dentatorubral-pallidoluysian atrophy. We present here a clinical course for this patient and discuss it.

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CLINICAL EXPERIENCE OF VIGABATRIN FOR PATIENTS WITH REFRACTORY EPILEPTIC SPASMS RESISTANT TO ADRENOCORTICOTROPIC HORMONE THERAPY

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Introduction: Vigabatrin (VGB) was approved for the treatment of epileptic spasms in Japan in 2016. However, clinical experience with the drug is limited in Japan, mainly because the special registry system is required to

ensure that the benefits of VGB outweigh its associated risk of visual loss.
Methods: We retrospectively analyzed the medical records of four patients (three female, one male) who received VGB in our hospital.
Results: The average age at registry for VGB therapy was 28 months (range, 12 to 50). Each patient exhibited a different underlying condition, including brain tumor complicated by hydrocephaly, chromosome abnormality associated with severe congenital cardiac malformations, GPI anchor deficiency, and hypoxic-ischemic encephalopathy. The average interval between adrenocorticotropic hormone (ACTH) therapy and the initiation of VGB therapy was 3.2 months (range, 2 to 4). The average number of antiepileptic drugs prescribed before the initiation of VGB therapy was 3.7 (range, 2 to 7). Only one patient (25%) achieved a seizure-free status. Despite reduced cone b-wave and 30 Hz flicker amplitudes in the electroretinograms of this patient, her parents hoped to continue VGB therapy because she was almost completely blind before its initiation. The remaining three patients presented no adverse effects.
Discussion: VGB is typically used as a second-line treatment for epileptic spasms that are resistant to ACTH therapy. In addition to a previous study conducted in Japan, this study showed limited efficacy of VGB, although the drug remains a therapeutic choice for patients who cannot receive surgical treatment due to underlying diseases.

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BRAIN MAGNETIC RESONANCE IMAGING ABNORMALITIES ASSOCIATED WITH VIGABATRIN: TWO CASES OF INFANTILE SPASM

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OBJECTIVE: To examine MRI abnormalities of patients with infantile spasm (IS) undergoing vigabatrin treatment.
METHODS AND RESULTS: We describe two cases of IS with MRI abnormalities induced by vigabatrin. Case 1: The patient is a 10-month-old boy. He had Ohtahara syndrome at 1 month and had IS at 3 months. We treated him with vitamin B6, some antiepileptic drugs, and ACTH therapy. However the effect of these treatments was temporary. At 10 months, we treated him with vigabatrin. The treatment was effective, but two months later, there were asymptomatic brain abnormalities on MRI signal changes in the bilateral thalami, basal ganglia, and brainstem. We reduced vigabatrin, and the MRI abnormalities disappeared after 8 months. Case 2: The patient is a 6-month-old boy. He had tuberous sclerosis complex and developed IS at 3 months. We treated him with vigabatrin, but treatment was not effective. Six days after the start of ACTH therapy, his tonic spasms disappeared. However, from day 8 he lost energy and showed right side hemiplegia. There were also brain abnormalities shown on MRI. We stopped the treatment of vigabatrin, and his symptoms improved.
Conclusion: Prior studies suggest a possible association between symptomatic MRI abnormalities and coadministration of hormonal therapy and vigabatrin. In our cases, the patient, case 2, with combination therapies of vigabatrin and ACTH had symptomatic MRI abnormalities; and the patient, case 1, without combination therapies had no symptoms. We suggest not using vigabatrin and ACTH at the same time.

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A CASE OF AGENESIS OF THE CORPUS CALLOSUM AND EPILEPSY WITH A SUPPRESSION-BURST PATTERN WITHOUT CHORIORETINAL LACUNAE: AICARDI-LIKE SYNDROME

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[Introduction] Aicardi syndrome (AS) is a rare disease that presents with agenesis of the corpus callosum (ACC), infantile spasm and chorioretinal lacunae (CL). We experienced a case of ACC with some features of AS without CL.
[Case Report] A 19-month-old girl born at 41 weeks' gestation (birth weight and head circumference: 2,550 g and 33.8 cm, respectively) showed ACC from the fetal period. Generalized tonic-clonic seizures occurred at 3 days old, and we noted a suppression-burst pattern (SBP) with split brain on electroencephalogram (EEG). Her seizures disappeared following the administration of phenobarbital. She also had hypotonia, deficit of the left 12th rib, and congenital hip dislocation. Brain magnetic resonance imaging (MRI) at 8 days old presented complete ACC. We suggested AS, but she had no CL. At 19 months old, she had intellectual disability (developmental quotient 40) and no attack of seizures. EEG at 12 months old showed a split-brain pattern, multifocal paroxysms, no SBP and no hypsarrhythmia.
[Discussion] The clinical features of our case matched some of the diagnostic criteria of AS, such as ACC, EEG findings and rib abnormality; however, no CL or infantile spasm was noted. ACC without AS presents with milder clinical feature than that with AS. Our findings suggest that there is a disease group with characteristics similar to AS (Aicardi-like syndrome).
[Conclusion] It is important to perform an ophthalmologic examination for patients with ACC to distinguish it from AS and elucidate the pathogenies of ACC and similar disorders.

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A PATIENT WITH VERY RARE SYNDROME: ALAZAMI SYNDROME

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Introduction: Alazami syndrome is an autosomal recessive disease with depletion or loss of function variants in LARP7 gene. To date, only 15 patients and two additional siblings have been reported. Case presentation and results: A 16 years old male patient admitted to the outpatient clinic with the complaint of autistic behaviour, flushing of ears, tachycardia and sweating attacks. His mother and fathers are cousen degree relatives. On his physical examination, he has growth and developmental retardation, prominent forehead, deep set eyes, low set ears, sparse eye brows, broad nose, short philtrum, low set ears, upper limb joint mobility, thickened skin over the hands and feet. He is also oversensitive to the noise. Genetic examination with whole exome sequencing revealed that he has homozygote variation in LARP7 gene. Both her mother and father has heterozygote for that variant. The patient's variant describes the clinic profile of the patient according to literature and database. Conclusion: Our case report describes this rare genetic condition. The disase is characterized with growth restriction, intellectual disability and dysmorphic features. Our patient has autonomic dysfunction and autistic behaviour additionally. We thought that, those would contribute the widening the disease profile.

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A CASE OF CHROMOSOME 8P INVERTED DUPLICATION DELETION SYNDROME WITH INFANTILE SPASMS AND SEVERE DEVELOPMENTAL DELAY

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[Introduction] Chromosome 8p inverted duplication deletion syndrome (invdupdel[8p]) is a complex chromosome 8 rearrangement with a prevalence of 1/10,000-30,000 newborns. Its clinical manifestations include mental retardation, hypoplasia or agenesis of the corpus callosum, characteristic facial appearance, congenital heart disease, orthopedic abnormalities, and hypotonia. This syndrome consists of a deletion distal to the 8p23 region followed by an intermediate intact segment, and a proximal inverted duplication of various extensions. [Case & Result] We report a 1-year-old boy who experienced symptoms of epileptic spasms from age 8 months and electroencephalogram detected hypsarrhythmia . He was diagnosed with infantile spasms and his symptoms disappeared after intramuscular low-dose adrenocorticotropic hormone therapy. He showed dysmorphic facial appearances, coarctation of the aorta, hypotonia, and severe developmental delay. Magnetic resonance imaging detected hypoplasia of the corpus callosum. Because his chromosome analysis (G-banding, Fluorescence in situ hybridization, and Spectral karyotyping) revealed deletion of 8p subtelomeric region and proximal inverted duplication, he was diagnosed with invdupdel(8p) at 1 year of age. To understand the genetic background of this case, we performed Microarray-based comparative genomic hybridization. Array study showed the presence of a 8p23.3-pter deletion and a duplication from 8p11.21 to 8p23.2. This case had no intact segment between duplicated and deleted regions, which have not been reported in the patients with invdupdel(8p). [Conclusion] This is the first case of invdupdel(8p) with infantile spasms. The genes located at the large size of inverted duplication might be associated with infantile spasms and severe neurodevelopmental phenotypes.

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A CASE OF TYROSINE HYDROXYLASE (TH) DEFICIENCY: CLINICAL COURSE WITH ORAL TREATMENT

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Introduction: TH deficiency is a rare disease characterized by infantile seizure-like involuntary movements, and there is few report described treatments except levodopa therapy. The severe case of TH deficiency is not always cured by levodopa. Here, we describe the clinical course of our patient during 4 year follow up period.
Patient: A 4 year and 6month old girl. At 3 months of age, she exhibited bilateral ptosis, spontaneous movement from the neonatal period. She had paroxysmal irritability, moisis, and sleep disturbance. Neurological examinations revealed involuntary movement (dystonic movement of the lips and limbs), bilatetal ptosis, and hypotonia. Oculogyric crisis appeared at 5 month of age. A trial treatment with levodopa/carbidopa was initiated at the 8 months of age, leading to the relief of ptosis, oculogyric crisis, dystonic movement and other symptoms. Dopa-responsive dystonia was suspected, and sequence analyses of TH gene showed compound heterozygosity for two mutations, c.698G>A and c.1141-1G>A. Ptosis, oculogyric crisis, moisis, sleep disorder were disappeared with the increase of levodopa/carbidopa dose, but spontaneous dystonic movements were remained. For dyskinesias according to the increments of levodopa, we divided levodopa/carbidopa to 3-5 doses, and decreased levodopa dose to the previously tolerated dose. Amantadine and zonisamide(ZNS) were added for insufficient control of the dyskinesias. Additional amantadine improve her talking abilities, and ZNS lead to

decrease of contventional levodopa dose.
Conclusion: Our patient showed an improvement of her dyskinesias with amantadine and ZNS. These drugs are alternative treatment when control of the dyskinesias is insufficient in the patient with TH deficiency.

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AN INFANT WITH DIETARY VITAMIN B12 DEFICIENCY DUE TO MATERNAL ANTIBODIES PRESENTING WITH WEST SYNDROME

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[Introduction] West syndrome is a unique age-related epileptic disorder affecting infants. Many conditions had been associated with this heterogeneous epilepsy syndrome, such as early brain insult, chromosomal anomalies, and genomic mutations. Inborn errors of metabolism are relatively uncommon etiology of West syndrome.
[Method & Results] The proband was a boy of 7 months of age, born to healthy non-consanguineous parents. Although he developed normally for the first 5 months, he had lost developmental milestones, and became hyporesponsive. At 7 months of age, recurrent episodes of head nodding occurred in clusters. He was exclusively breast-fed by his mother with normal diet. Interictal EEG showed hypsarrhythmia pattern, and MRI revealed cerebral atrophy. Laboratory tests showed non-macrocytic anemia, methylmalonic aciduria, homocystinuria, low serum methionine, and profoundly low vitamin B12 level. The symptom-free mother without atrophic gastritis had macrocytosis, low vitamin B12 level and positive anti-internal factor and anti-parietal cell antibodies. Intramuscular adrenocorticotropic hormone and vitamin B12 replacement were initiated and proved to be effective in seizure control. Development was evaluated as low as 13 months at 20 months of age.
[Conclusions] Epilepsy is a rare clinical manifestation of infantile vitamin B12 deficiency, although few reports had described the association with West syndrome. None of the 5 reported infants showed neurodevelopment delay at last follow-up. The severe level and presumed long period of vitamin B12 deficiency might have resulted irreversible neurological damage. Vitamin B12 deficiency should be suspected in exclusively breast-fed infants presenting with West syndrome.

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PERAMPANEL AND KETOGENIC DIET IN WEST SYNDROME DUE TO NEONATAL NONKETOTIC HYPERGLYCINEMIA: A CASE REPORT

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Nonketotic hyperglycinemia appears as a severe form of early onset epileptic encephalopathy due to disturbance of glycine cleavage system. Glycine acts as an excitatory neurotransmitter via the *N*-methyl-D-aspartate (NMDA) receptor. The combination therapy with dextromethorphan and sodium benzoate are reported to be effective for seizures, however, seizures usually remain uncontrolled. In this report, we describe a case of nonketotic hyperglycinemia and discuss the treatment strategy of the seizure.
A 1-day-old Japanese boy presented with lethargy, profound hypotonia, and apnea which required mandatory ventilation for one month. At the 36th day he presented with hiccups, and 41th day epileptic spasms appeared. The EEG showed hypsarrhythmia and he was diagnosed with West syndrome. The brain MRI showed cortical dysplasia and corpus callosum agenesis. The CSF / serum glycine ratio was increased and he was diagnosed with nonketotic hyperglycinemia. Vigabatrine, ACTH therapy, and the combination of dextromethorphan and sodium benzoate were ineffective. By 9 months of age, perampanel reduced the epileptic spasms more than 50%. At age 1 year 2 month, ketogenic diet therapy dramatically reduced the focal seizure and the glycine level in CSF.
NMDA receptor activates prolonged electrical depolarizations after the fast excitatory neuronal activity, mainly induced by the α-amino-3-hyroxy-5-methyl-4-isoxazole propionic acid (AMPA) receptor, which is blocked by perampanel. Furthermore, ketogenic diet was not only useful for seizure reduction but also reduced glycine in CSF, which was reported previously. This case indicates that addition of perampanel and ketogenic diet may improve seizure control and quality of life in nonketotic hyperglycinemia.

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A CASE OF FATAL LEGIONELLA PNEUMONIA DURING ACTH THERAPY FOR WEST SYNDROME

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Legionella pneumophila is a rare cause of pneumonia in children, with case being reported among

immunodeficient patients and neonates. Although adrenocorticotropic hormone (ACTH) is effective for the treatment of infantile spasms, suppressions of immune function is a major adverse effects. We describe an 11-month-old girl with infantile spasms treated with ACTH who presented with fatal Legionella pneumonia. She was diagnosed with cerebral palsy due to hypoxic-ischemic encephalopathy caused by neonatal asphyxia. A series of epileptic spasms occurred at the age of 7 months, at which time electroencephalography revealed hypsarrhythmia. Treatment with VPA, ZNS, NZP, and VGB was conducted without improvement. Low-dose intramuscular ACTH therapy was started at the age of 10 months. One month after initiation of ACTH therapy, she developed refractory pneumonia leading to acute respiratory distress syndrome, sepsis, and multisystem organ failure. Although she was treated in the ICU with antibiotics, mechanical ventilation and extracorporeal membrane oxygenation, she died 8 days later. Legionella pneumophila serotype 3 was detected from sputum culture after her death. Our experience suggests that patients on ACTH therapy can develop severe infections, including with unusual pathogens, even with a short course of treatment. Legionella must be considered in patients receiving ACTH who develop pneumonia.

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A CHILD WITH MOVEMENT DISORDER MIMICKING SEIZURE IN GNAO1 RELATED ENCEPHALOPATHY

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GNAO1 gene encodes the a-subunit of heterotrimeric guanine nucleotide-binding protein (Gi protein), a membrane protein which widely expressed in the central nervous system involved in signal transduction. It may involve in inhibition of neurotransmitter release in synaptic level. In recent years, GNAO1 mutation was found to cause encephalopathy that consisted of severe early-onset hyperkinetic syndrome with or without epileptic encephalopathy. At times, movement disorders in these patients are hard to distinguish from seizures. In the present study, we described a 1.5 years old boy with motor developmental delay and movement disorder that mimicked seizure due to a de novo mutation of GNAO1. The patient had an uneventful birth history, however there was motor development delay with marked hypotonia, first noticed at about 6 months of age. Intermittent involuntary eye movements including eye deviation and upward gaze lasing several seconds noted since 8 months of age. He was suspected to have seizures which prompted EEG examination that revealed no concomitant epileptiform discharge. Other movement disorders such as chorea movement over bilateral arms. There was no dystonia. Series studies, including CSF and metabolic studies showed inconclusive results. Eventually, a de novo GNAO1 mutation was found using a targeted next generation sequencing gene panel. In conclusion, our study demonstrated that GNAO1 mutation related encephalopathy could result in encephalopathy with movement disorder that mimic seizure. Careful evaluation is mandatory to distinguish between these conditions.

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DYT1 EARLY-ONSET ISOLATED DYSTONIA

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It follows a pattern of autosomal dominantly (AD) inherited movement disorder that is manifested by involuntary twisting of different body regions, intermittent or continuous movements and abnormal postures without other neurological symptoms, signs, and secondary causes. DYT1 early-onset isolated dystonia often begins in childhood and adolescence with rare occurrence in adulthood. The symptom commonly starts from lower limbs and frequently propagates to other body regions when the disease progresses (1).

DYT1 early-onset isolated dystonia is a severe form of primary (or idiopathic) torsion dystonia (PTD or ITD) with an age of onset younger than 28 years old and a penetrance rate around 30 to 40% (2). Here, we report a boy who first exhibited waddling gait followed by fast development of typical dystonia. We surveyed candidate genetic alterations as well as the rates of AD carrier and the penetrance of his family to examine the proband effect.

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NEONATAL ABNORMAL MOVEMENTS FOLLOWED BY INFANTILE SPASMS CAUSED BY THE KCNQ2 R198Q MUTATION

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KCNQ2 gene mutations cause benign familial neonatal epilepsy, Ohtahara syndrome, and infantile spasms. We report an infant with a KCNQ2 mutation (codon 593 G>A; p. R198Q, de novo). In the neonatal period, she did not exhibit epileptic seizures but did display irritability and abnormal movements (a combination of transient hypertonia, jerks, and tremor-like movements, running from the neck to the upper limbs). These movements deteriorated from 2 to 4 months after birth. Diazepam was somewhat effective. She developed infantile spasms 5 months after birth, and was then treated with adrenocortical-stimulating hormone and sodium valproate. At 14 months of age, she remains seizure-free on sodium valproate monotherapy, but exhibits severe developmental delay. The KCNQ2 R198Q mutation has been reported in patients experiencing infantile spasms but not neonatal seizures. However, abnormal movements

caused by KCNQ2 R198Q have not been previously reported. Such movements in the neonatal period may be useful for early diagnosis of KCNQ2-associated encephalopathy.

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A CASE OF EARLY INFANTILE-ONSET LEIGH SYNDROME WITH A M.9185T>C IN THE MTATP6 GENE MUTATION COMPLICATED WITH INFANTILE SPASMS

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<Introduction>Leigh syndrome (LS) is the most common pediatric presentation of mitochondrial disease. LS is caused by various genetic defects including m.9185T>C mutation in MTATP6 gene. The clinical phenotype of m.9185T>C mutation is variable, including late-onset LS. Till date, early infantile-onset LS with m.9185T>C mutation complicated with infantile spasms have never been reported.

<Case>A girl was born at term(Apgar score5/6). Immediately after birth, she suffered from apnea, hypotonia, and feeding difficulty. Mechanical ventilation was necessary for 2 days.

At 4 months, she exhibited convulsions. The lactate levels were increased. Brain magnetic resonance imaging (MRI) and MR spectroscopy showed bilateral lesions in basal ganglia, cerebral peduncle and lactate peak. She was diagnosed as having LS.

At 6 months, she developed clustered spasms. In ictal electroencephalogram, generalized high-amplitude slow waves with spasms were consistent with Infantile spasms. Then we started adrenocorticotropic hormone (ACTH) therapy. ACTH therapy was effective for spasms, but blood lactate levels had been increased and brain atrophy had progressed. A mitochondrial DNA analysis showed homoplasmic de novo m.9185T>C mutation.

<Discussion>Our patient exhibited more severe symptoms and an earlier age of onset than observed in the previous reports of m.9185T>C mutations. Hence, we believe that m.9185T>C mutation demonstrated broad spectrums and ACTH therapy against Infantile spasms complicated with LS should be considered carefully.

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A PATIENT WITH LENNOX-GASTAUT SYNDROME CAUSED BY PACS2 GENE MUTATION

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Objective: We found the heterozygote mutation of PACS2 gene in a patient with Lennox-Gastaut syndrome (LGS) and autistic spectrum disorder (ASD) who had suffered from epilepsy since infancy. Patient: She is a 12-year-old girl. She was born at term to nonconsanguineous parents. She had facial dismorphism including hypertelorism and broad nasal root. Convulsions appeared at the day of three. She repeated generalized tonic-clonic convulsions which sometimes progressed to status. She was medicated with several anticonvulsants. EEG demonstrated the focal spikes. MRI findings were normal. Her intellectual and movement development were delayed. She was diagnosed as ASD and severe intellectual disability. Absence appeared at age of six. The interictal EEG demonstrated characteristic appearance of LGS with slow spike and wave and rapid rhythms. We analyzed her whole-exome sequence and found the de-novo heterozygote mutation of PACS2 gene. Now she can walk, though her muscles are hypotonus. She can speak words, but she cannot make conversations and her words are mostly echolalia. Epilepsy is controlled by lamotrigine, clonazepam and valproic acid. Discussions: PACS2 gene has roles in both the nucleus and cytoplasm. PACS2 controls the cell cycle in the nucleus, and regulates endoplasmic reticulum homeostasis, mitochondria communications, autophagy, and endosomal trafficking of ion channels, receptors and enzymes in cytoplasm, which leads to cerebellar dysgenesis and epilepsy. Reported patients had epilepsy controlled with difficulty in the first year, but many improved in early childhood. In our case, epilepsy occurred in infancy and it developed to LGS. And she has no abnormalities in cerebellum.

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NOVEL COMPOUND HETEROZYGOUS MUTATION OF THE TBC1D24 GENE IN A TAIWANESE INFANT WITH MULTIFOCAL MYOCLONUS AND EPILEPSIA PARTIALIS CONTINUA

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Advances in molecular genetic technologies have improved our understanding of infantile myoclonic seizures caused by Tre2-Bub2-Cdc16 (TBC) 1D24 mutations. Herein, we report the case of a male infant who presented first with nystagmus, ophthalmoplegia, and early-onset myoclonus and subsequently with multifocal myoclonus, epilepsia partialis continua, and developmental delay. Numerous laboratory and neuroimaging studies failed to identify the cause. To determine the underlying etiology, we conducted whole-

exome sequencing.

We identified a novel compound heterozygous mutation in the TBC1D24 gene [c.119G>A (p.Arg40His); c.1499C>T (p.Ala500Val)]. Although TBC1D24 has been associated with disorders encompassing various neurophenotypes of a mostly autosomal recessive type, the combination of known and novel TBC1D24 variants in our patient further demonstrated its clinical manifestation as a phenotypic spectrum. Compiling and analyzing more cases of TBC1D24 mutations is necessary to explore the clinical spectrum of TBC1D24-associated disorders.

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A CASE OF *SCN1A*-RELATED EPILEPSY CHARACTERIZED BY REPEATED EPISODES OF SEIZURES IN CLUSTER INDUCED BY FEVER, RESEMBLING *PCDH19*-RELATED EPILEPSY

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[Background] *SCN1A* encodes the voltage-gated sodium channel ($Na_v1.1$) α1 subunit. Epileptic syndromes associated with *SCN1A* mutation include a variety of phenotypes, such as familial febrile seizures, genetic epilepsy with febrile seizures plus, and Dravet syndrome. We herein report a case of *SCN1A*-related epilepsy that expands the epilepsy phenotypes. [Case report] The patient, an 11-month-old boy, presented with repeated seizures in cluster induced by fever, which needed management in the intensive care unit. He recovered with no sequela leading to a diagnosis of complex febrile seizures. He was given diazepam suppositories for the prevention of febrile seizures, but seizures in cluster repeated in association with fever. These episodes resemble *PCDH19*-related epilepsy. Gradually, he also presented afebrile convulsions even under treatment with valproate sodium and levetiracetam. His electroencephalogram showed sharp waves in the right frontal lesion, while brain MRI showed no abnormality. His motor and cognitive development was normal. Whole exome sequencing identified a novel missense mutation in *SCN1A* gene, c.811G>A(p.Gly271Ser). [Discussion] Clinical phenotypes of *SCN1A*-related epilepsy are related to the age at seizure onset. The present patient had late onset of seizure at 11 months of age, compatible with such milder clinical phenotype. [Conclusion] Seizures in cluster are observed in patients with *SCN1A*-related epilepsy as well as those with *PCDH19*-related epilepsy. This finding expands epilepsy phenotypes associated with *SCN1A*-related epilepsy.

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A CASE OF DEVELOPMENTAL AND EPILEPTIC ENCEPHALOPATHY CAUSED BY A NOVEL SCN2A GENE VARIAN

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Variants in SCN2A, which encodes a subunit of voltage-gated sodium channels (Na v1.2), cause benign familial neonatal-infantile seizures, generalized epilepsy febrile seizure plus, and early-onset epileptic encephalopathy. We report a 10-month old girl with developmental and epileptic encephalopathy (DEE) carrying a novel SCN2A variant. After uneventful delivery, she developed apneic episodes and tonic seizures at 1-day old. phenobarbital, diazepam and levetiracetam were ineffective to control her seizures. Intravenous midazoram was temporarily effective. Then, clobazam (CLB) was begun at 32-days old; CLB 0.7mg/kg/day abolished her seizures. Ictal video EEG showed that her seizures originated from each hemisphere. Her brain MRI revealed no abnormality. After obtaining informed consent from her parents, we performed targeted capture sequencing on 198 genes for DEE using next generation sequencer, which identified a novel de novo missense variant in SCN2A (c.4021C>G, p.Leu134Val). In silico analysis (SIFT and PolyPhen-2) predicted that this variant is deleterious or probably damaging. This was not listed in public databases. We concluded that this SCN2A variant was causative in the patient. Although CLB is ineffective in all 6 patients with DEE caused by SCN2A variant previously, CLB efficacy might be unique in our patient.

P-40

A CASE OF SCN8A-ASSOCIATED EPILEPTIC ENCEPHALOPATHY CAUSED BY A NOVEL HETEROZYGOUS MUTATION: WHERE IS THE ORIGIN OF REFRACTORY STARTLE REFLEX AND MYOCLONUS?

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Introduction: SCN8A gene encodes the neuronal voltage-gated sodium channel Nav1.6. Recently, mutations of SCN8A have been shown to be associated with epileptic encephalopathy. Herein we report a case of SCN8A-associated epileptic encephalopathy caused by a novel heterozygous mutation. The patient presented with refractory epilepsy coexisting with refractory startle reflex and myoclonus. We performed electrophysiological studies to investigate the mechanism of each symptom.

Case: A term newborn male presented with a history of startle reflex and spontaneous myoclonic movements starting shortly after birth and development of generalized tonic seizures at the age of two days. Subsequently, he exhibited severely delayed psychomotor development and continued to suffer from refractory epilepsy and startle reflex and myoclonus. Brain magnetic resonance imaging (MRI) in early infancy revealed almost normal findings; however, MRI performed at the age of nine months showed signs of cerebral atrophy and delayed myelination. The clinical course and presentation were consistent with epileptic encephalopathy. Whole exome sequencing analysis revealed de novo and novel heterozygous mutation c.4436T> C: (p.Ile1479Thr) in SCN8A gene. Ictal electroencephalography (EEG) revealed that the seizure originated in the cerebral cortex. The results of electrophysiological studies such as somatosensory evoked potential, C-reflex studies, and EEG did not always indicate that refractory startle reflex and myoclonus were derived from the cerebral cortex.
Discussion: In this patient, mutation of SCN8A may not only have increased the excitability of cerebral cortex but may also have affected the subcortical or spinal neuronal circuits.

P-41

CORPUS CALLOSOTOMY FOR EPILEPTIC SPASMS OR TONIC SEIZURES IN PATIENTS WITH TUBEROS SCLEROSIS COMPLEX

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Background: Corpus callosotomy (CC) is a surgical procedure for the patients with intractable epilepsy, who are not the candidate of cortical resection. The procedure achieves seizure freedom in 43% of ACTH-resistant, non-lesional West syndrome patients. We report the CC cases of tuberous sclerosis complex (TSC) with bilateral multiple lesions.
Method: We retrospectively collected the patients: 1) diagnosed as TSC, 2) had intractable epileptic spasms or tonic seizures, and 3) received CC for those seizures in our hospital between November 2014 and December 2018. We evaluated data of clinical information, MR images, and the seizure outcomes.
Results: Totally 7 patients (4 women) received total CC between 2-21 year-old (median, 3). The target seizures of CC were epileptic spasms in 6 and tonic seizures in one patients, respectively. Each 2 patient coincided with partial seizures or atypical absences. The cognitive developments were severely delayed in 4, moderately in one, and mildly in 2. All patients showed bilateral cortical tubers (>10) on MR images. Two of the patients underwent additional resection surgery, and one patient received preceding implantation of vagus nervous stimulation. Finally, 4 patients (CC only, 3; CC + resection, 1) achieved seizure freedom. Three of them were better cognitive development (mild, 2; moderate, 1). Three patients did not show worthwhile seizure reduction.
Conclusion: CC might be a good treatment for intractable epileptic spasms in the patients with bilateral lesions in tuberous sclerosis complex. Non-severe cognition might be the good prognostic factor.

P-42

PALLIATIVE HEMISPHEROTOMY IN AN INFANT WITH NEONATAL-ONSET INTRACTABLE EPILEPSY ASSOCIATED WITH EXTENSIVE CEREBRAL DYSPLASIA

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We report the case of a male infant who had neonatal-onset intractable epilepsy associated with bihemispheric cerebral dysplasia with left-side dominance, and who underwent a palliative hemispherotomy with a successful outcome. The infant had an uneventful delivery, but had numerous focal seizures daily starting on the first day of life. He also had epileptic spasms from 4 months of age. At 8 months of age, his development was severely delayed with right hemiplegia without head control. He often experienced seizure clustering, which required admission. All available antiepileptic medication was ineffective to control his seizures. Prolonged video-electroencephalogram (VEEG) monitoring confirmed that the origin of the focal seizures was exclusively the left hemisphere. Although the patient was not an ideal candidate for hemispherotomy, which would leave pathology with the possibility of remaining seizures, we performed surgery with the informed consent from his parents to alleviate his disabling seizures. After surgery, his original seizures disappeared, and the family did not notice any apparent clinical seizures in daily life. The infant began to smile, and there was a definite improvement in his development and quality of life. Although VEEG showed that he often had brief crying episodes that were associated with focal seizure activity originating from the right hemisphere, they were clinically mild with no disturbance in his activity. This case shows that, even though cerebral dysplasia is extensive and involves bilateral hemispheres, a palliative hemispherotomy of the more affected side can be an option to improve the patient's quality of life.

P-43

DEVELOPING MICE MODEL OF ACUTE ENCEPHALOPATHY USING LOW-DOSE LIPOPOLYSACCHARIDE INJECTION AND HYPERTHERMIA TREATMENT: A SIMPLE AND CONVENIENT METHOD

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Purpose: Currently, the pathogenesis of acute encephalopathy (AE) is unclear and one of the reasons for this is a lack of a simple and convenient animal model. In this study, we hypothesized that AE has a pathogenesis of systemic inflammation and hyperthermia (HT). Materials and methods: Postnatal, 8-day-old mouse pups were intraperitoneally injected with low-dose lipopolysaccharide (LPS, 50 or 100 µg/kg) followed by HT treatment (41.5°C, 30 min). Subsequently, their brains were histologically analyzed. Fluorescein isothiocyanate combined with immunohistochemistry was used to elucidate blood-brain barrier (BBB) disruption. Results: LPS (100 µg/kg) injection followed by HT treatment increased BBB permeability in the cerebral cortex and induced microglial activation. Additionally, astrocytic clasmatodendrosis was evident. Brains of some pups exhibited small ischemic regions, particularly in the cerebral cortex. Conclusion: These results indicate that low-dose LPS injection followed by HT treatment can produce symptoms of cytokine storm-induced AE, which is observed in diseases such as acute necrotizing encephalopathy and hemorrhagic shock and encephalopathy syndrome. We believe that this mouse model can help elucidate pathogenetic mechanisms underlying AE.

P-44

EARLY DIFFERENTIATION OF ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION FROM FEBRILE STATUS EPILEPTICUS USING EEG ANALYSIS

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Objects: To differentiate acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) from febrile status epilepticus (FS) using the cross-spectrum analysis of encephalography (EEG) data. Methods: We retrospectively collected data from 18 children who had status epilepticus and from whom EEGs were recorded within 26 hours. These included patients with a final diagnosis of AESD (n = 9) and FS (n = 9). We performed cross-spectrum analysis to calculate the phase lag value of EEG signals between two electrodes. Additionally, we constructed a time-frequency map using cross spectrum values for analyzing the time-frequency correlations between two time series from a single patient. Electrodes were placed according to the international 10-20 system using at least 10 channels (Fp1, Fp2, F3, F4, C3, C4, P3, P4, O1, and O2) and interhemispheric phase lag was analyzed. Six representative, artifact-free 10-second epochs were selected from each record and average phase lag values were calculated. Results: The AESD group showed higher phase lag values at F3-F4 in the delta and gamma bands and at C3-C4 in the beta band than the FS group. The alpha phase lag values of these groups were not significantly different. Moreover, the time-frequency maps of the AESD group showed higher phase lag values at all areas in all frequency bands. However, the maps of the FS group depicted strong synchronism in only the delta band. Conclusions: The phase lag of EEG signals at frontal areas may be useful for the early diagnosis of AESD.

P-45

A CASE OF INFLUENZA ASSOCIATED ENCEPHALOPATHY WITH LATE REDUCED DIFFUSION OBSERVED SURROUNDING PRE-EXISTING FOCAL CORTICAL LESION

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Pathophysiology of acute encephalopathy with biphasic seizure and late reduced diffusion (AESD) remains uncertain. Excitotoxicity has been suggested as possible pathomechanism based on elevated glutamine and glutamate complex on MR spectroscopy. We describe a boy with delayed subcortical diffusion surrounding pre-existing focal cortical lesion after prolonged convulsion triggered with Influenza virus infection. High fever and cough appeared 1 day prior to admission. The following day, prolonged seizure lasted 50 minutes. Electroencephalogram revealed spike-and-wave complex on left frontal pole with left dominant delta activity. Rapid nasal swab was positive for Influenza A virus antigen. Head MR imaging on admission day showed focal cortical lesion suspected focal cortical dysplasia in the left frontal lobe without diffusion abnormality. Due to prolonged impaired consciousness more than 12 hours, therapeutic hypothermia was initiated. Diffusion-weighted MR imaging on day 6 revealed reduced diffusion in the subcortical white matter on left frontal lobe

surrounding focal cortical lesion. Ictal EEG demonstrated intractable seizure or status epilepticus around focal lesion of left frontal lobe, and this support the hypothesis of excitotoxicity causing reduced subcortical diffusion in the affected area. To our knowledge, there is no previous report describing subcortical delayed reduced diffusion which appeared only surrounding pre-existing focal cortical lesion.
In conclusion, our case suggests that putative epileptic cortical lesion can be a risk factor of AESD, and preceding influenza virus infection may act as a potential epileptic instigating agent of focal lesion.

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ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION: COMPARISON BETWEEN INFLUENZA AND HHV6/7

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Background. Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is the most common subtype of acute encephalopathy in Japan. AESD is characterized by an early seizure on day 1, typically status epilepticus, late seizures on day 4 to 6, usually a cluster of focal seizures, and subsequent neurologic sequelae including severe epilepsy. The most common pathogenic virus is HHV6/7, followed by influenza virus. The aim of this study was to clarify any differences between influenza and HHV6/7 cases in clinical symptoms, neuroimaging findings and outcome. Methods. We collected clinical information of patients with AESD from hospitals in Japan from 2008 to 2018. Then we analyzed the clinical data of HHV6/7 and influenza associated cases. Results. Among 258 AESD cases, 89 cases were associated with HHV6/7 and 27 with influenza. Median age at onset was 13 months in HHV6/7 and 37 months in influenza. Age at onset was significantly higher in influenza ($P = 2.0 \times 10^{-8}$). In HHV6/7, biphasic seizures were significantly more common ($P = 0.003$), whereas status epilepticus as the early seizure was comparable between the two. The outcome and radiological lesions showed no significant differences between HHV6/7 and influenza. Conclusions. Except for differences in the age at onset and time course of seizures, the clinical picture of AESD was quite similar between HHV6/7 and influenza associated cases.

P-47

ACUTE ENCEPHALOPATHY WITH NONCONVULSIVE STATUS EPILEPTICUS IN ROTAVIRUS GASTROENTERITIS

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Acute encephalopathy (AE) is a generic term for acute brain dysfunction, usually preceded by infection without inflammatory cells in the brain and cerebrospinal fluid. The main symptoms are disturbed consciousness and convulsion. In addition to classic AE caused by metabolic errors, several syndromes have been recently established based on the clinicopathological or clinicoradiological features, including acute necrotizing encephalopathy (ANE) and AE with biphasic seizures and late reduced diffusion (AESD). Whereas, it has been postulated that cytokine storm and excitotoxicity underlie ANE and AESD, respectively, and the pathogenic mechanisms remain unknown in many cases. Here, we report two cases (a 3-year-old girl and a 4-year-old girl) of AE, wherein nonconvulsive status epilepticus was considered the leading cause of neurological symptoms and propose a novel clinicoelectroencephalographi cally defined AE syndrome. In both cases, long-term electroencephalographically (EEG) monitoring was performed to evaluate impaired consciousness in the course of rotavirus-positive gastroenteritis. Bilateral 3 Hz high-amplitude slow waves with occipital predominance fluctuated with the consciousness level. Immediately after intravenous benzodiazepine infusion, the paroxysmal waves completely disappeared with drastic improvement in consciousness. After short-term oral anticonvulsant administration, they survived without epileptic seizures for 10 years and 1 year, respectively. The etiology was identical in both the cases; therefore, rotavirus may play an important role for temporally driving thalamocortical circuits in early childhood. However, its specificity in the etiology must be validated with further investigations because the diagnosis could be missed without long-term EEG monitoring in other infections.

P-48

ASSOCIATION OF RARE NONSYNONYMOUS VARIANTS OF *SCN1A* WITH ACUTE ENCEPHALOPATHY WITH BIPHASIC SEIZURES AND LATE REDUCED DIFFUSION

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Purpose. Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is characterized by biphasic febrile seizures and a delayed appearance of subcortical white matter lesions. The pathogenesis is suspected to be excitotoxicity leading to neuronal death. *SCN1A* and *KCNQ2* are causative genes of genetic epilepsy including Dravet and Otahara syndrome. Here we conducted a case-control rare-variant association study of the two genes in AESD.
Methods. The Sanger sequencing of the coding regions

of *SCN1A* and *KCNQ2* was performed on 175 and 111 AESD patients respectively. As control subjects, we used Integrative Japanese Genome Variation Database of Tohoku Medical Megabank Organization. Then we performed a case-control association study of rare nonsynonymous variants (sample MAF < 0.005) of each gene with AESD using a burden test (WSS: Weighted Sum Statistics) and a variance component test (SKAT: Sequence Kernel Association Test).
Results. *SCN1A* rare variants had a significant association with AESD in both tests after correction for multiple tests (WSS, permutated p value 0.003: SKAT, p value 0.00025: α= 0.05/2 gene sets). Although *KCNQ2* rare nonsynonymous variants tended to be more common in patients than in controls, there was no significant difference (WSS, permutated p value 0.35: SKAT, p value 0.056: α= 0.025)
Conclusions. Our study first provided statistical evidence of an association between *SCN1A* and AESD, and established *SCN1A* as one of the susceptibility genes for AESD.

P-49

INFLUENZA-ASSOCIATED CNS COMPLICATIONS IN FEBRILE CHILDREN: ELEVATED ALT MAY BE AN EARLY HINT OF ACUTE NECROTIZING ENCEPHALOPATHY

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Object:
To investigate the prevalence rate of liver involvement in pediatric patients with influenza-associated complications and its role in the early detection of influenza-associated acute necrotizing encephalopathy (ANE).

Methods:
During January 1st 2010 to December 30th 2017, 64 febrile pediatric patients who were admitted to a tertiary medical center due to influenza-associated complications and had the results of blood alanine aminotransferase (ALT) were recruited. Patients were divided into the central nervous system (CNS) group and non-CNS group based on their indication of hospitalization. Demographic, clinical and laboratory data of both groups was recorded via retrospective chart reviews.

Results:
Most of patients were admitted due to secondary lung infection, gastrointestinal upset and myositis, while the others were admitted due to CNS complications, like seizure, visual hallucination and encephalitis. Patients in the CNS group had higher rate of liver involvement than those in the non-CNS group (21.7% vs 2.4%, p=0.02). In the CNS group, ANE patients had significantly higher rate of liver involvement, movement abnormality, central diabetes insipidus (DI) and mortality than non-ANE patients (p<0.05).
Conclusion:
In patients with influenza-associated CNS complications, liver involvement and movement abnormality may be the early hints for the diagnosis of ANE.

P-50

THREE CASES PRESENTING WITH TRANSIENT EDEMATOUS BRAIN LESIONS AFTER FEBRILE STATUS EPILEPTICUS

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<Introduction> Subtle brain lesions can be detected earlier when using magnetic resonance imaging (MRI) through application of diffusion-weighted imaging (DWI) and arterial spin labeling (ASL) methods after status epilepticus; this is important for the diagnosis of acute encephalopathy in children. Here, we describe three patients with transient edematous brain lesions, as shown by DWI, after febrile status epilepticus. We assessed the blood perfusion of the lesions by using a combination approach with ASL.
<Case summary> Intravenous antiepileptic drug delivery was needed for status epilepticus in all patients in this case series. DWI showed transient reduction of diffusion (days 4-7) in the precentral gyrus in two patients and in the hippocampus in one patient; in two patients, ASL revealed hyperperfusion of the lesions in the acute phase (days 4-7), while it showed hypoperfusion in the subacute phase (days 11-12). One patient showed hypoperfusion, antecedent to the DWI change, immediately after status epilepticus.
<Discussion> Edematous lesions after convulsions are found in the hippocampus and central sulcus; some of these exhibit hypofusion immediately after convulsion. We suspect that, because of the convulsions, neural metabolism is accelerated and blood flow shows a relative reduction; the blood flow may compensate for these changes. MRI can simultaneously evaluate brain parenchyma and blood flow without the risks inherent in radiation exposure and use of contrast medium. Therefore, MRI constitutes a convenient tool for diagnosis and follow-up of patients with transient edematous brain lesions after febrile status epilepticus.

P-51

ETIOLOGY AND NEUROIMAGING OF FEBRILE INFECTION-RELATED EPILEPSY SYNDROME (FIRES)

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Background:
Febrile infection-related epilepsy syndrome (FIRES) is characterized by refractory status epilepticus in previously healthy, school-aged children that presents itself with or just after a nonspecific febrile illness.
Methods:
During the period of 2016 January to 2018 July, we enrolled the patients who were eligible for FIRES, and patients of encephalitis/encephalopathy as a control group. We did the survey of antineuronal antibodies. Brain MRI was performed at the first and 6th months. At 6 months, the PET-MRI was arranged. We collected clinical data of patients, including age, sex, clinical symptoms, possible infectious pathogens, and prognosis.
Results:
There were 47 patients enrolled in this study, including 30 FIRES, and 17 non-FIRES. In the FIRES group, the presumed infectious pathogens were found as follows: EB virus (8), Mycoplasma pneumonia (5), Herpes simplex virus (8), Influenza virus (12). Anti-NMDAR antibody were found in 5 patients. At last visit, there were 17 patients on antiepileptic drugs treatment. Abnormal brain MRI were found in 13 (46.3%) patients. Most of the involved areas of brain were temporal lobes or brain atrophy. Brain PET-MRI were performed in 11 FIRES patients which showed decreased metabolism in temporal lobe (10) (7 bilateral and 3 left side), 6 frontal lobe (2 bilateral, 1 right, 3 left), and 2 occipital lobe (2 bilateral).
Conclusions:
In this study, we found that anti-NMDAR antibody play an important role in FIRES. Brain MRI and PET of FIRES had abnormal findings in 6 months follow-up. Further studies are necessary for long term outcomes.

P-52

TREATMENT AND SHORT-TERM PROGNOSIS OF CONVULSIVE REFRACTORY STATUS EPILEPTICUS IN CHILDREN

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Purpose: We aimed to investigate treatment and short-term prognosis of convulsive refractory status epilepticus (RSE) in children.
Methods: We retrospectively reviewed the medical records of 17 patients (9 boys) with convulsive RSE concerning the choice of antiepileptic drugs (AEDs) and neurological sequelae at the discharge as the short-term prognosis. Convulsive RSE was defined as convulsive status epilepticus which failed to response to adequately treated by benzodiazepines as the first-line therapy, such as diazepam and/or midazolam (MDL), and another AED as second-line.
Results: The median age at onset was 1.6 years (ranged from 0.2 to 12.3). The etiology was acute encephalopathy/encephalitis in 10, epilepsy in three (including Dravet syndrome in one), febrile seizures in two, and others in two (abused child and drowning in one each). The median duration of seizures was 100 minutes (ranged from 20 to 1200). The AEDs which ceased seizures finally was continuous MDL in eight, thiopental in seven, and phenobarbital and phenytoin in one each. As adverse effects, respiratory and circulatory disorder was found in 12 (70.6%) and six (35.3%), respectively. Concerning short-term prognosis, neurological sequelae were found in nine (52.9%): motor and intellectual disability in seven and eight, respectively. Death was found in only one with acute encephalopathy/encephalitis.
Conclusion: Continuous MDL and thiopental were effective drugs for pediatric convulsive RSE, and required cardio-respiratory supports. The short-term prognosis of this condition was unfavorable, especially in acute encephalopathy/encephalitis.

P-53

ENTEROVIRUS D68 NEUTRALIZING ANTIBODY IN CULTURE-NEGATIVE ACUTE FLACCID MYELITIS

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Introduction
Acute flaccid myelitis emerged with the prevalence of enterovirus D68 since 2014. Difficulties of enterovirus D68 isolation during the illness of acute flaccid myelitis further hamper the causal relationship establishment. In the study, we supposed that neutralizing assay of enterovirus D68 could reveal the etiology of pediatric acute flaccid myelitis with unrecognized viral pathogen.
Methods
Since November 2017 to November 2018, children diagnosed of acute flaccid myelitis in the hospital were retrospectively enrolled. The demographic data, neurological presentations, neuroimaging results, laboratory data, treatment modalities, and outcomes were reviewed.
Results
There were 7 girls and 10 boys with median age 2.8 years. Nine children had fever in the past 2 weeks. The first neurological symptom could be lower limb weakness, upper limb weakness, brainstem dysfunction, or sensory complaints. The neurologic status progressed to nadir after median 2 days with variable motor weakness of monoplegia, diplegia, and quadriplegia. The yield rate of viral culture was low, so was the PCR. Twelve patients had paired serum samples for enterovirus D68 neutralization tests; 5 had at least 4 folds of titer change and 1 showed persistent high titers. Significant enterovirus D68 neutralizing antibody in 6 of the 12 tested patients enhanced the diagnosis of enterovirus D68 associated acute flaccid myelitis in our series.
Conclusions
Enterovirus D68 neutralization assay could be the next laboratory strategy for pediatric acute flaccid myelitis with unknown causes.

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POST VACCINATION CONVULSION RARE IN BANGLADESH-A COMPREHENSIVE STUDY

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The Aim of the study is to find out if there is any true of the Myth of Convulsion- post vaccination. Specially Polio Vaccine oral or injectable form.

The Study was done in three well managed modern Medical Center in the Urban Area of Dhaka City, Bangladesh.

The Centers are Well Baby Clinic, Red Crescent Hospital, and Dhaka Shisu (Children) Hospital.

Time frame- January 1998 to December 2000.

Total Three thousand children, one thousand in each center were followed up.

Social status- all were well educate financially solvent family´s child, as the vaccination done on payment basis.

The vaccination was supervised by qualified Pediatrician.

Vaccines were given as per EPI -schedule at time prevailing in Bangladesh. Vaccine are BCG, DPT, Polio, Measeles,DT,Hepatitis -B , Chicken Pox etc.

Out Come- Out of all vaccination NOT a single child develops Convulsion or fits post vaccination.

Around 15 children develops mild fever, one child develops rash, three child develops mild abscess at the site of injection. Ten children develop diarrhea post oral polio vaccination.

Conclusion- Post Vaccination convulsion or Fit is rare in Bangladesh. But needs more multiple centers study.