International Symposium on

Biology of Seizure Susceptibility

The 10th Annual Meeting of the Infantile Seizure Society

PROGRAM & ABSTRACTS

April 7-8, 2007, Tokyo, Japan

Conference Hall

North Building, Mita Campus, Keio University

Sponsored by	Infantile Seizure Society (ISS), Japan
Co-Sponsored by	Japan Foundation for Neuroscience and Mental Health
Supported by	The Japan Epilepsy Society
	Japan Pediatric Society
	The Japanese Society of Child Neurology

CONTENTS

WELCOME MESSAGE

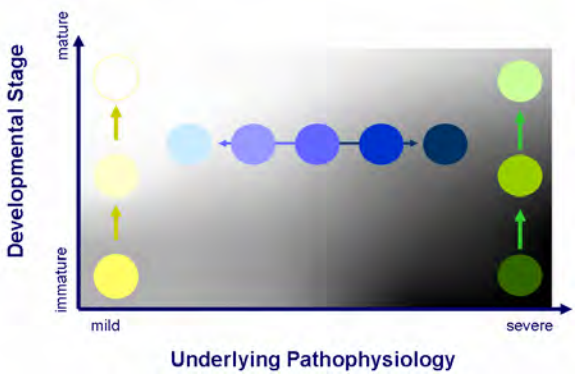
Dear colleagues,

Welcome to the International Symposium on Biology of Seizure Susceptibility!

In this symposium, explorations through comprehensive presentations and thorough discussion on such issues as morphogenesis, receptors and neurotransmitters, ion channels etc. are in prospect. I'm sure that the symposium will be an exiting and fruitful one for you as many distinguished physicians/scientists in the field of epileptology, developmental neurobiology and others are invited to give a lecture. It will certainly be a wonderful opportunity for you to discuss all aspects of seizure susceptibility during neonatal and infantile period.

The framework or general scheme of the symposium may be viewed as shown in the following figure with two axes: the abscissa representing various kinds of underlying pathophysiology of variable degree in its severity whereas the ordinate representing the neurodevelopmental stages, both governing the seizure susceptibility during the neonatal and infantile period. Factors involved in the underlying pathophysiology will include race/gender, malnutrition, receptors/ion channels, dysgenesis, pharmacokinetics of AED, acute illnesses/inflammation and many others.

Within this framework, seizure susceptibility may be simplified as the overlaid gradation shade: the lower right corner being the highest susceptibility while the upper left corner being the lowest. At a given developmental stage with variable degree of underlying pathophysiology, seizure susceptibility is expected to vary accordingly as indicated with blue circles. As shown with a dark green circle, an individual with devastating underlying pathology such as grave malformations of the CNS is likely to have very high susceptibility to seizures at his/her early stage of neural development: seizure susceptibility is expected to change as the person gets older, usually to become less, that is, the green circle moves upwards. Another example may be seen as with yellow circles where an apparently healthy infant has higher seizure susceptibility than adults but as the person grows the seizure susceptibility may "disappear".



Underlying biology that governs the age dependent seizure susceptibility is the main theme of the meeting. Those of you who agree with or at least are interested in this framework are certainly our guests. Those who do not agree with or see substantial revisions to be made to this framework are strongly encouraged to participate in the discussion at this meeting.

All the best,

Takao TAKAHASHI, MD, PhD
President,
International Symposium on Biology of Seizure Susceptibility,
The 10th Annual Meeting of Infantile Seizure Society
Professor and Chairperson,
Department of Pediatrics, Keio University School of Medicine

ORGANIZATION

ORGANIZING COMMITTEE

[A] GENERAL

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[B] SCIENCEIFIC PROGRAM COMMITTEE

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Committee Members

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Osamu KANAZAWA (Saitama, Japan)
Shin-ichi NIIJIMA (Tokyo, Japan)
Akihisa OKUMURA (Tokyo, Japan)
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Hitoshi YAMAMOTO (Kawasaki, Japan)

[C] FUND COMMITTEE AND TREASURER

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Committee Members

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Shinichi NIIJIMA (Tokyo, Japan)
Hirokazu OGUNI (Tokyo, Japan)
Hitoshi YAMAMOTO (Kawasaki, Japan)
Hideo YAMANOUCHI (Tochigi, Japan)

SPONSORING ORGANIZATIONS

Sponsor	Infantile Seizure Society (ISS), Japan
Co-sponsor	Japan Foundation for Neuroscience and Mental Health
Support	The Japan Epilepsy Society Japan Pediatric Society The Japanese Society of Child Neurology

SECRETARIAT FOR ISBSS

Secretary General	Keiichi YAMAMOTO, MD
Secretariat	Department of Pediatrics, Keio University School of Medicine 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan Phone: +81-3-3353-1211 ext. 62365 Fax: +81-3-5379-1978 Email: iss2007eng@yahoo.co.jp
Secretary Staff	Fujiyo ARIMA, Tomohide GOTO, Akiko KAMIISHI, Takayuki MITSUHASHI, Sahoko MIYAMA, Hirohiko OZAKI, Sachiko SHIMOZATO

GENERAL INFORMATION

DATE

April 7th (Saturday) - April 8th (Sunday), 2007

VENUE

Conference Hall, North Building, Mita Campus, Keio University, Tokyo, Japan
Phone: +81-3-3453-4511

Oral presentations: at the Conference Hall in the North Building (2nd floor),
Poster presentations: in the Corridor (2nd floor).
Smoking is prohibited in the entire North Building. Drinking and eating in the Conference Hall is also prohibited.

OFFICIAL LANGUAGE

English only. No simultaneous translation available.

SOCIAL FUNCTION

Grand Social Party

Date & Time:	18:30-20:30, Saturday, April 7th
Place:	North Building, Cafeteria (1st Floor)
Attire:	Casual
Attendance:	Registration required

OFFICIAL CERTIFICATE for ATTENDANCE and CME CREDITS

An official certificate for attendance at the ISBSS will be delivered to all foreign participants.
For Japanese colleagues, a certificate for authorized CME units will be rewarded by the two societies as follows:

Society	Attendance	Authorship	
		Presenter	Co-author
Japan Pediatric Society	5 U	0 U	0 U
The Japanese Society of Child Neurology	2 U	2 U	0 U

U = unit

LUNCH (Days 1 and 2)

Lunch will be served for participants for free at the Cafeteria on the 1st floor. Please present a coupon attached to your name card. Please take your lunch within the Cafeteria.
Many other restaurants are also available near the Mita campus.

COFFEE and SNACKS

Coffee and snacks will be served at the 2nd floor (free).

MEETING of the ISS OFFICERS

12:20-13:20, Saturday, April 7th
Conference Room on the 4th floor, North Building

SATELLITE BUSINESS MEETING

The Asian & Oceanian Child Neurology Association (AOCNA) Executive Board Meeting
13:00-18:00, Friday, April 6th
Headquarters Office on the 2nd floor, North Building

To MAKE YOUR STAY COMFORTABLE

CLIMATE

April is the most comfortable season of the year in Tokyo area with high temperature being around 20 degree Celsius (68 degree Fahrenheit) and low around 10 degree Celsius (50 degree Fahrenheit).

CURRENCY EXCHANGE

We strongly recommend purchasing yen at Narita Airport. This is because you need cash in yen to purchase tickets for ground transportation from the airport to wherever your first destination in downtown Tokyo may be. Moreover, most of the banks are closed on Saturday and Sunday thus you may not be able to change your currency to yen.

VOLTAGE and FREQUENCY of ELECTRICITY

The voltage is 100 V throughout the country. Frequency is 50 Hz in Tokyo area and 60 Hz in the western Japan such as Kyoto or Osaka.

SHOPPING

Five percent sales tax is applicable to personal purchases. Duty free shops are available at Narita International Airport, Haneda Airport, and qualified electronics and computer stores in Akihabara area in Tokyo (15 min from the venue by train, for 160 yen).

GRATUITY / TIP

Gratuity or “service fee” is included in a bill at most of the descent restaurants. Otherwise they usually do not accept any tips.

SIGHTSEEING TOURS

If you wish to have a sightseeing tour during your stay in Japan, we recommend making a reservation in advance through travel agency such as Sunrise Tour, a subsidiary company operated by Japan Travel Bureau.
Please visit their web site at http://www.jtbgmt.com/sunrisetour/.
If you have any questions, please contact to ISBSS secretariat.

SECRETARIAT

Inquiries on ISBSS 2007:

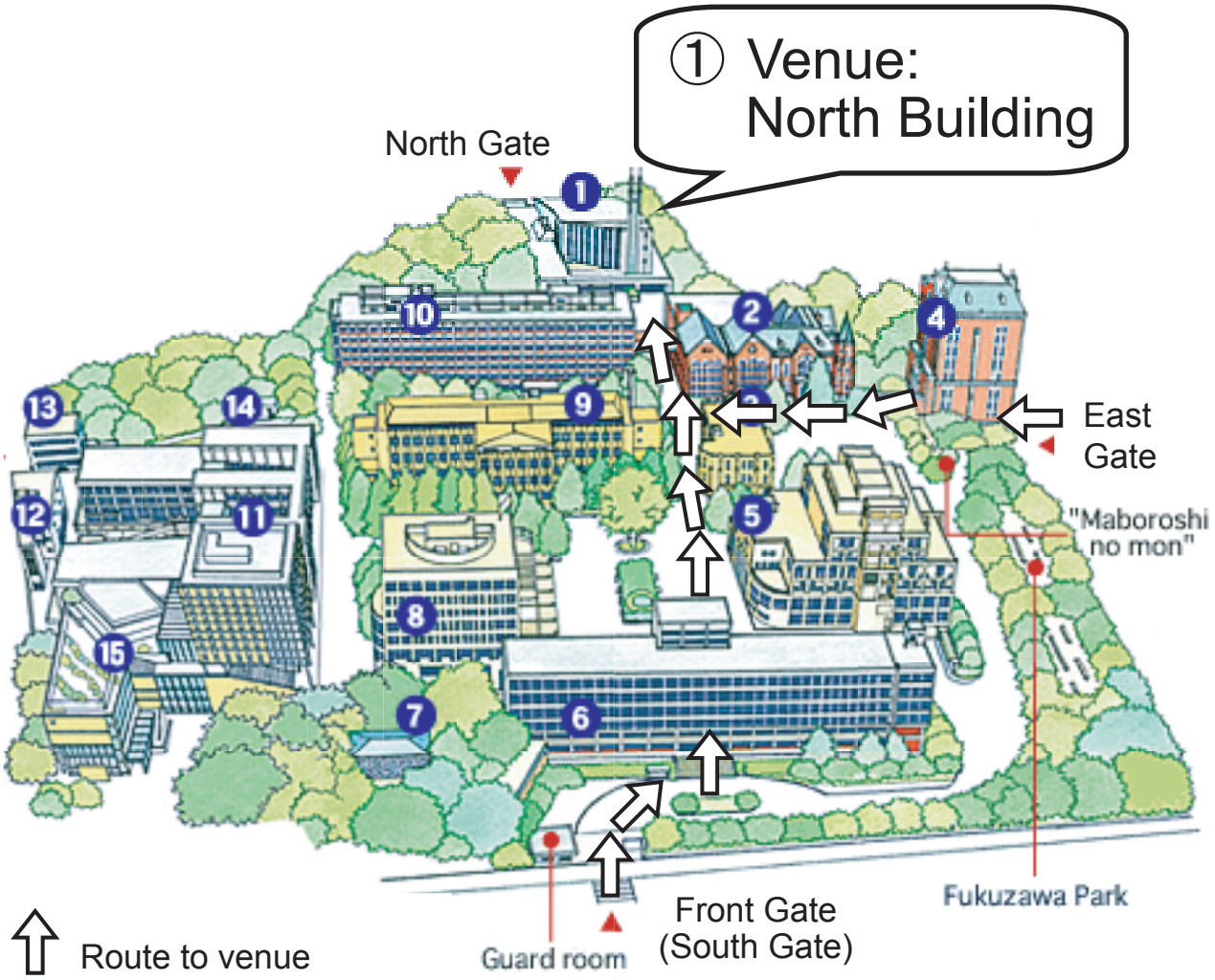
ISBSS Secretariat
Takao Takahashi, MD, PhD
Professor and Chairperson
Department of Pediatrics, Keio University School of Medicine
35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan
Phone: +81-3-3353-1211 ext 62365
Fax: +81-3-5379-1978
Email: iss2007eng@yahoo.co.jp

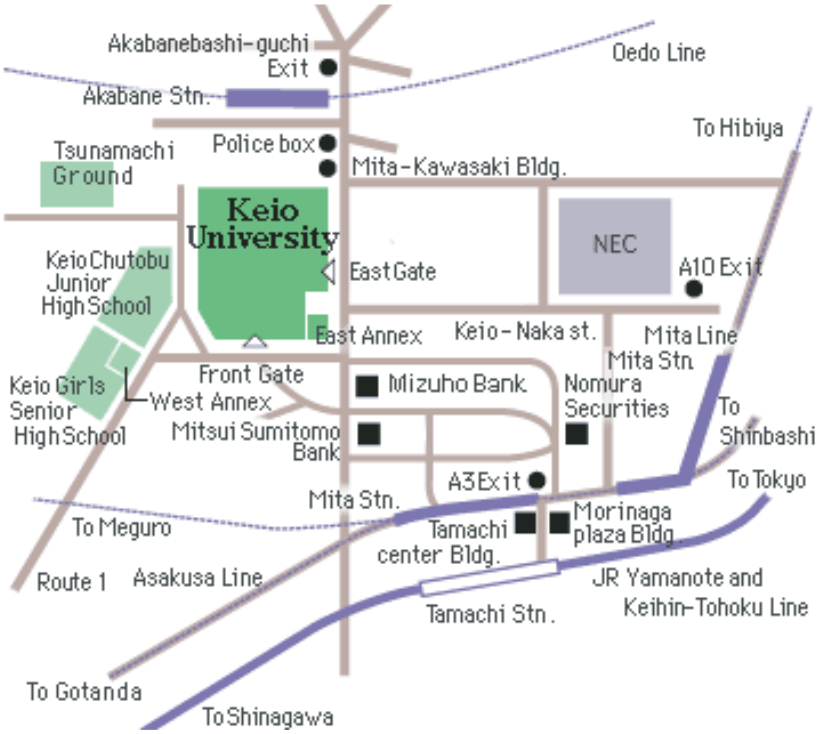
Inquiries on Infantile Seizure Society in general:

ISS Secretariat
Yukio Fukuyama, MD, PhD
c/o Child Neurology Institute
6-12-17-201 Minami-Shinagawa, Shinagawa-ku, Tokyo
140-0004, Japan
Phone: +81-3-5781-7680
Fax: 81-3-3740-0874
Email: yfukuyam@sc4.so-net.ne.jp

ISS/ISBSS Website http://www.iss-jpn.info/

VENUE INFORMATION: MITA CAMPUS MAP



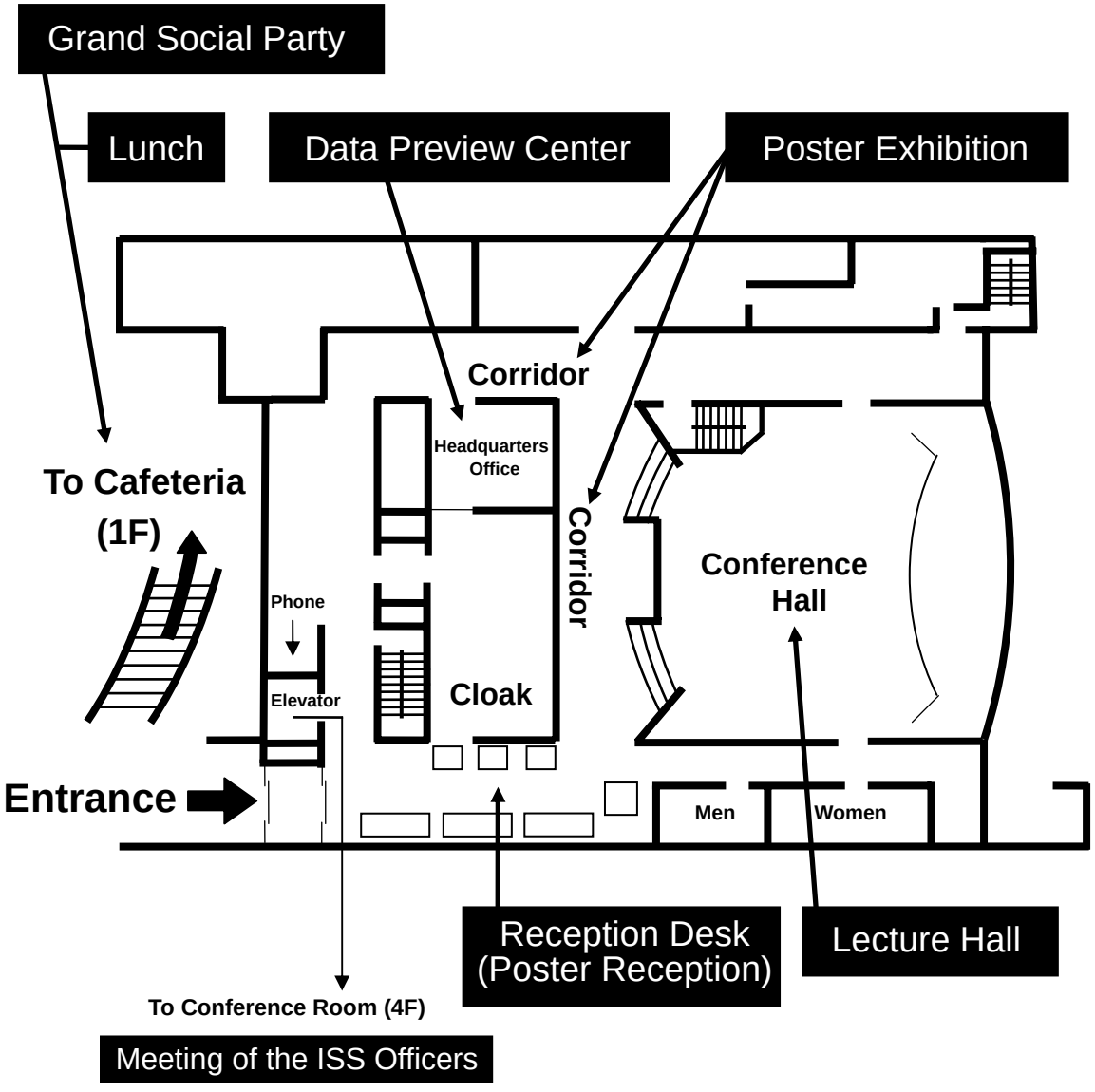


Address:
2-15-45 Mita, Minato-ku, Tokyo
108-8345
Phone:
+81-(0)3-3453-4511

- An 8-minute walk from Tamachi Station (JR Yamanote Line or JR Keihin-Tohoku Line)
- A 7-minute walk from Mita Station (Subway Asakusa Line or Subway Mita Line)
- An 8-minute walk from Akabanebashi Station (Subway Oedo Line)

FLOOR PLAN

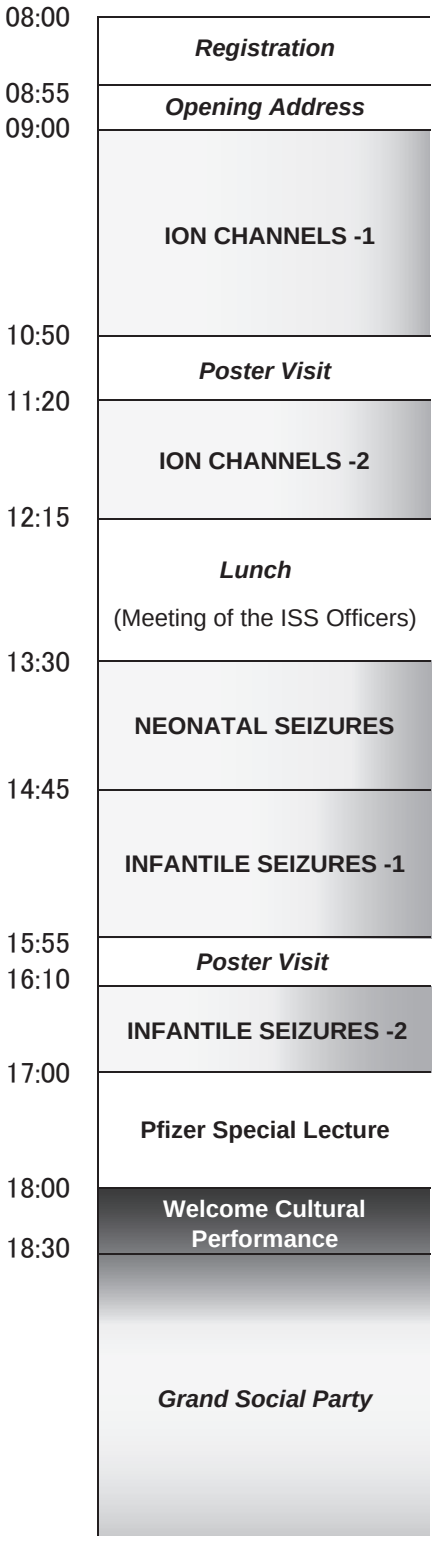
2F, North Building



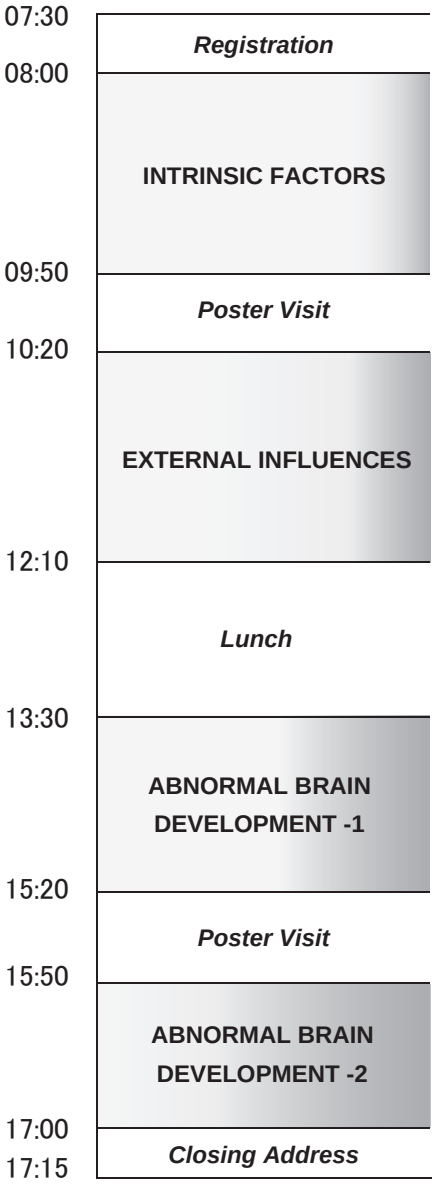
Eating and drinking are prohibited in the Conference Hall.
No smoking in the building.

OVERVIEW of DAILY PROGRAM

Day 1, Saturday April 7



Day 2, Sunday April 8



REGISTRATION

Desk for Registration and General Information, located on the 2nd floor at the Conference Hall, North Building, will be open during the following periods:

Day 1, April 7th (Saturday)	08:00-18:30
Day 2, April 8th (Sunday)	07:30-17:00

PRE-REGISTERED

Those who made the registration on-line should go to the Pre-registrant Reception Desk, present a copy of Registration Confirmation email and receive a ready-prepared bag.

ON-SITE REGISTRATION

Fill out the upper part of the Registration Form and present it to the Reception Desk with the payment as listed below in cash in Japanese yen.

Note: all in Japanese Yen (JP¥), ISS = Infantile Seizures Society, AOCNA = Asian & Oceanian Child Neurology Association.

Symposium

Japanese colleagues		
ISS member	21,000	JP¥
Non-ISS member (Japanese only)	24,000	JP¥
Non-Japanese colleagues		
AOCNA member (Japanese not included)	18,000	JP¥
Non-AOCNA member (Japanese not included)	24,000	JP¥

Grand Social Party (Day 1, April 7th)	5,000	JP¥

To ISS MEMBERS

The members of the Infantile Seizures Society (ISS) are requested to pay annual fees (3,000 JP¥) at the Registration Desk. To become a member of ISS, please fill out the membership application form and pay the 2007 annual fee (3,000 JP¥).

To AOCNA MEMBERS

The members of the Asian & Oceanian Child Neurology Association (AOCNA) are requested to contact with the AOCNA reception desk, and confirm his/her correspondence address in the membership roster and status of due payment.

To become an AOCNA MEMBER

Please fill out the application form and pay the two-year-fee for the years 2007-2008 (20 US$) or the whole life fee (100 US$) in cash.

DON'T MISS THE GRAND SOCIAL PARTY

Let's get together at the Grand Social Party at the Cafeteria, North Building (1st floor) on Saturday evening, April 7th. It offers an ideal opportunity to meet with old as well as new friends and enjoy traditional Japanese hospitality.

INSTRUCTION

FOR ORAL PRESENTATIONS

1. **Data Preview**
   Be in contact with a staff at least two hours before the presentation and preview your presentation at the Data Preview Center (2nd floor, North Building). For those who give a lecture in the morning it is advised to contact with a staff the day before.
2. **Slide Projection**
   A single projection will be available. Windows-operated computers will be prepared by the organizer. Bring your presentation file either on a USB flash memory or CD-R.
3. **Time for Discussion**
   Please note the time allocated for each presentation is as follows;
   40 minutes for presentation followed by 15 minutes of discussion for invited speakers and 15 - 20 minutes for presentation followed by 5 minutes of discussion for others.

FOR POSTER PRESENTATIONS

1. **Registration**
   The poster presenter is requested to register at the "Poster Reception Desk" on the 2nd floor, North Building.
2. **Poster Exhibition**
   Posters should be up on the pre-assigned panel in the Corridor of the 2nd floor, North Building by 9:00 AM, Day 1 (April 7th). Pushpins will be provided.
3. **Poster Visit**
   Presenters are requested to be present at the site of respective posters for discussion during the time as specified below:

   Poster number 1 through 5 (Cell Biology / Pathology) and
   Poster number 10 through 15 (Cytokine / Infectious Disease)

   → Day1 (April 7th) Poster Visit and Coffee Break (10:50-11:20)
   Poster Visit and Coffee Break (15:55-16:10)

   Poster number 6 through 9 (Genetics) and
   Poster number 16 through 27 (Epilepsy, Neuroimaging)

   → Day2 (April 8th) Poster Visit and Coffee Break (09:50-10:20)
   Poster Visit and Coffee Break (15:20-15:50)

PROGRAM

The 10th Annual Meeting of the Infantile Seizure Society

International Symposium on Biology of Seizure Susceptibility

PROGRAM - ORAL PRESENTATIONS

DAY 1, SATURDAY, APRIL 7

08:00-18:30 **REGISTRATION**

08:55-09:00 **OPENING ADDRESS**

Takao TAKAHASHI (President of ISBSS, the 10th Annual Meeting of ISS, 2007)

09:00 **ION CHANNELS - 1**

Chairperson: Yoshihiro TAKEUCHI (Shiga, Japan)

Ulrich SCHRIDDE (New Haven, USA)

ORAL 1 10th ISS **09:00–09:55** INVITED

Molecular pathogeneses of epilepsy resulting from channel dysfunction

Shinichi HIROSE (Fukuoka, Japan)

ORAL 2 10th ISS **09:55-10:50** INVITED

Functional effects of sodium channel mutations that cause GEFS+

Alan L. GOLDIN[1], Karoni DUTT[1], Arthur J. BARELA[1], Jay SPAMPANATO[1,3], Bin TANG[2], Andrew ESCAYG[2] ([1]Irvine, [2]Atlanta, [3]Los Angeles, USA)

10:50-11:20 **Poster Visit and Coffee Break** POSTER 10th ISS

11:20 ION CHANNELS - 2

Chairperson: Makiko OSAWA (Tokyo, Japan)

Paolo CURATOLO (Rome, Italy)

ORAL 3 10th ISS

11:20-12:15 INVITED

Clinical expressions of ion channel epilepsy disorders

Alexis ARZIMANOGLOU (Paris, France)

12:15-13:30 Lunch

12:20-13:20 Meeting of the ISS Officers

13:30 NEONATAL SEIZURES

Chairperson: Kazuyoshi WATANABE (Aichi, Japan)

Alexis ARZIMANOGLOU (Paris, France)

ORAL 4 10th ISS

13:30-13:50

Risk factors for postneonatal epileptic seizure in the newborns with neonatal seizures

Hiroshi OTSUBO, Sang-Ook NAM, Ayako OCHI, O. Carter SNEAD III (Toronto, Canada)

ORAL 5 10th ISS

13:50-14:45 INVITED

Recent Advances in the treatment of neonatal seizures

Kevin J. STALEY (Boston, USA)

14:45 INFANTILE SEIZURES - 1

Chairperson: Kazuie IINUMA (Miyagi, Japan)

Harvey B. SARNAT (Calgary, Canada)

ORAL 6 10th ISS

14:45-15:40 INVITED

The vulnerability of the hippocampal neurons to infantile seizures

John W. SWANN (Houston, USA)

ORAL 7 10th ISS

15:40-15:55

Genetic susceptibility to febrile seizures: interleukin-10 attenuates febrile seizures susceptibility

Yoshito ISHIZAKI[1], Ryutaro KIRA[1], Mitsumasa FUKUDA[2], Hiroyuki TORISU[1], Masafumi SANEFUJI[1], Naoko YUKAYA[1], Mariko IWAYAMA[1], Toshiro HARA[1]
([1]Fukuoka, [2]Ehime, Japan)

15:55-16:10 **Poster Visit and Coffee Break** POSTER 10th ISS

16:10 INFANTILE SEIZURES - 2

Chairperson: **Takeki FUJIWARA (Shizuoka, Japan)**

Veena KALRA (New Delhi, India)

ORAL 8 10th ISS

16:10-16:25

ARX mutation in females: an under-recognized cause of epilepsy and developmental delay

Amanda W. PONG, Yaman Z. EKSIOGLU, Masanori TAKEOKA
(Boston, USA)

ORAL 9 10th ISS

16:25-16:40

A longer polyalanine expansion mutation in the ARX gene causes OHTAHARA syndrome

Mitsuhiro KATO[1], Shinji SAITOH[2], Atsushi KAMEI[3], Hideaki SHIRAISHI[2], Yuki UEDA[2], Manami AKASAKA[3], Jun TOHYAMA[4], Noriyuki AKASAKA[4], Kiyoshi HAYASAKA[1]
([1]Yamagata, [2]Sapporo, [3]Morioka, [4]Niigata, Japan)

ORAL 10 10th ISS

16:40-16:55

Distinct clinical course of SMEI with SCN2A mutation - Comparison with SCN1A mutations

Hitoshi OSAKA[1], Emi MAZAKI[2], Nami OKAMURA[2], Sumimasa YAMASHITA[1], Mizue IAI[1], Michiko YAMADA[1], Kazuhiro YAMAKAWA[2]
([1]Yokohama, [2]Wako, Japan)

17:00-18:00 **Pfizer Special Lecture**

Sponsored by Pfizer Japan Inc.

ORAL 11 10th ISS

Factors influencing the choice of treatments in epilepsy

Solomon L. MOSHÉ (New York, USA)

Chairperson: Tallie Z. BARAM (Irvine, USA)

Shunsuke OHTAHARA (Okayama, Japan)

18:00-18:30 **WELCOME CULTURAL PERFORMANCE**

***Nihon Buyo* (Japanese Classical Dance)**

'*Echigo Jishi*', performed by Junomaru HANAYAGI

18:30-20:30 **GRAND SOCIAL PARTY**

Venue: the Cafeteria, North Building (1st floor)

Registration required for participation

DAY 2, SUNDAY, APRIL 8

07:30-17:00 **REGISTRATION**

08:00 **INTRINSIC FACTORS**

Chairperson: Shinichi NIIJIMA (Tokyo, Japan)

Alan L. GOLDIN (Irvine, USA)

ORAL 12 10th ISS

08:00-08:55 INVITED

Linking biochemical pathways to seizure susceptibility in early life: lessons from inborn errors of metabolism

Asuri PRASAD, Chitra PRASAD (London, Canada)

ORAL 13 10th ISS

08:55-09:50 INVITED

Gender influences on the maturation of endogenous systems involved in seizure control

Solomon L. MOSHÉ (New York, USA)

09:50-10:20 **Poster Visit and Coffee Break** POSTER 10th ISS

10:20 **EXTERNAL INFLUENCES**

Chairperson: Teruhisa MIIKE (Kumamoto, Japan)

Kevin J. STALEY (Boston, USA)

ORAL 14 10th ISS

10:20-11:15 INVITED

How stress early in life enhances seizure susceptibility

Tallie Z. BARAM (Irvine, USA)

ORAL 15 10th ISS

11:15-12:10 INVITED

How nurture shapes nature: the role of the environment on the development of seizure activity

Ulrich SCHRIDDE[1,2], Gilles VAN LUIJTELAAR[2]

([1]New Haven, USA, [2]Nijmegen, Netherlands)

12:10-13:30 **Lunch**

13:30 ABNORMAL BRAIN DEVELOPMENT - 1

Chairperson: Kenji SUGAI (Tokyo, Japan)

John W. SWANN (Houston, USA)

ORAL 16 10th ISS

13:30-14:25 INVITED

Genetic malformations of the cerebral cortex and seizure susceptibility during infancy

Ganeshwaran H. MOCHIDA (Boston, USA)

ORAL 17 10th ISS

14:25-15:20 INVITED

Fetal synaptogenesis and infantile epilepsies

Harvey B. SARNAT, Laura FLORES-SARNAT (Calgary, Canada)

15:20-15:50 **Poster Visit and Coffee Break** POSTER 10th ISS

15:50 ABNORMAL BRAIN DEVELOPMENT - 2

Chairperson: Hirokazu OGUNI (Tokyo, Japan)

Asuri N. PRASAD (London, Canada)

ORAL 18 10th ISS

15:50-16:45 INVITED

Seizure susceptibility in tuberous sclerosis complex: molecular pathogenesis and rationale for treatment

Paolo CURATOLO (Rome, Italy)

ORAL 19 10th ISS

16:45-17:00

Evolution of EEG in young infants in tuberous sclerosis complex

Sergiusz JOZWIAK, Dorota DOMANSKA-PAKIEŁA, Joanna SZYMKIEWICZ-DANGEL, Jolanta KASPRZYK-OBARA (Warsaw, Poland)

17:00-17:15 CLOSING ADDRESS

Yoshihiro TAKEUCHI (President of ISFS, the 11th Annual Meeting of ISS, 2008)

The 10th Annual Meeting of the Infantile Seizure Society

International Symposium on Biology of Seizure Susceptibility

PROGRAM - POSTER PRESENTATIONS

DAY 1, SATURDAY, APRIL 7

Poster Number 1 through 5 (Cell Biology / Pathology)

and

Poster Number 10 through 15 (Cytokine / Infectious Disease)

10:50-11:20 Poster Visit and Coffee Break

15:55-16:10 Poster Visit and Coffee Break

DAY 2, SUNDAY, APRIL 8

Poster Number 6 through 9 (Genetics)

and

Poster Number 16 through 27 (Epilepsy, Neuroimaging)

09:50-10:20 Poster Visit and Coffee Break

15:20-15:50 Poster Visit and Coffee Break

CELL BIOLOGY / PATHOLOGY

Poster Visit
Day 1

POSTER 1 10th ISS **GABA promotes the differentiation of newborn dentate granule cells**
Junya ICHIKAWA, Yuji IKEGAYA, Norio MATSUKI, Ryuta KOYAMA
(Tokyo, Japan)

POSTER 2 10th ISS **Effects of the ketogenic diet on the brain-derived neurotrophic factor expression after kainic acid-induced seizures in young mice**
Ho Jin PARK[1], Dong Wook KIM[2]
([1]Daejeon, [2]Goyang, Korea)

POSTER 3 10th ISS **Early-life seizure induces an emergence of ectopic granule cells in adult mice dentate gyrus**
Rieko MURAMATSU, Yuji IKEGAYA, Norio MATSUKI, Ryuta KOYAMA
(Tokyo, Japan)

POSTER 4 10th ISS **Altered distribution of KCC2 in cortical dysplasia in patients with intractable epilepsy**
Mitsutoshi MUNAKATA[1], Mika WATANABE[2], Taisuke OTSUKI[3], Hideyuki NAKAMA[3], Kunimasa ARIMA[4], Masayuki ITOH[5], Junichi NABEKURA[6], Kazuie IINUMA[1], Shigeru TSUCHIYA[1]
([1,2]Sendai, [3,4,5]Tokyo, [6]Okazaki, Japan)

POSTER 5 10th ISS **Nonfunctional SCN1A is common in severe myoclonic epilepsy in infancy**
Iori OHMORI[1], Kris M KAHLIG[2], Thomas H RHODES[2], Dao W WANG[2], Mamoru OUCHIDA[3], Hideki MATSUI[1], Alfred L GEORGE Jr[2]
([1,3]Okayama, Japan, [2]Nashville, USA)

GENETICS

Poster Visit
Day 2

POSTER 6 10th ISS **Frequencies of single nucleotide polymorphisms of the multidrug resistance 1 gene in Korean population**
Young Ok KIM[1], Myeong Kyu KIM[2], Young Jong WOO[1], Min Cheol LEE[3], Jin Hee KIM[2]
([1,2,3]Gwangju, Korea)

POSTER 7 10th ISS **Association of GABRG2 polymorphisms with idiopathic generalized epilepsy**
I-Ching CHOU[1], Chang-Hai TSAI[1,2], Lei WAN[3], Yu-An HSU[3], Tsai-Chung LEE[4], Fuu-Jen TSAI[1,3]
([1,2,3,4]Taichung, Taiwan)

POSTER 8 10th ISS **Mental retardation and neuropsychiatric symptoms in a female with compression in the first polyalanine tract of the ARX gene**

Yaman Z. EKSIOGLU, Amanda PONG, Masanori TAKEOKA
(Boston, USA)

POSTER 9 10th ISS **West syndrome in a girl with compression in the second polyalanine tract of the ARX gene**

Yaman Z. EKSIOGLU, Amanda PONG, Masanori TAKEOKA
(Boston, USA)

CYTOKINE / INFECTIOUS DISEASE

Poster Visit
Day 1

POSTER 10 10th ISS **Influences of interleukin-1β on the propensity of hyperthermia-induced seizures in developing rats**

Mitsumasa FUKUDA[1], Chiya SHINONAGA[1], Takehiko MORIMOTO[2], Yuka SUZUKI[3], Yasushi ISHIDA[1]
([1,2]Ehime, Japan, [3]New York, USA)

POSTER 11 10th ISS **Withdrawn**

POSTER 12 10th ISS **A comparison with provoked seizures and febrile seizures associated with minor infections**

Eun Ju LEE, Won Seop KIM
(Cheongju, Korea)

POSTER 13 10th ISS **Status epilepticus induced by respiratory syncytial virus infection in preterm infants**

Mi-Sun YUM[1], Su Jeong YOU[2], Tae-Sung KO[1]
([1]Ulsan, [2]Inje, Korea)

POSTER 14 10th ISS **ACTH therapy in infantile spasms and cytomegalovirus infection**

Dorota DUNIN-WASOWICZ, Sergiusz JOZWIAK, Jolanta KASPRZYK-OBARA
(Warsaw, Poland)

POSTER 15 10th ISS **Cluster seizures with diarrhea in infancy: norovirus infection in an endemic area**

Hsiu-Fen LEE, Ching-Shiang CHI, Chou-Huei CHEN, Po-Yen CHEN, Fang-Liang HUANG, Chieh-Chung LIN
(Taichung, Taiwan)

Poster Visit

Day 2

EPILEPSY

POSTER 16 10th ISS

A clinical study of acute symptomatic seizures in children

Keon-Su LEE[1], Won-Seop KIM[2]
([1]Daejeon, [2]Cheongju, Korea)

POSTER 17 10th ISS

Early infantile epilepsies: seizure types and evolutions

Motomasa SUZUKI[1], Kazuya ITOMI[2], Kiyokuni MIURA[3], Hiroyuki KIDOKORO[4], Tetsuo KUBOTA[4], Toru KATO[1], Fumio HAYAKAWA[1], Akihisa OKUMURA[5], Koichi MARUYAMA[6], Yoko KONDO[7], Jun NATSUME[7], Kazuyoshi WATANABE[8]
([1]Okazaki, [2]Obu, [3]Kasugai, [4]Anjo, [5]Tokyo, [6,7]Nagoya, [8]Aichi, Japan)

POSTER 18 10th ISS

Overall prognosis of ACTH therapy for West syndrome

Yoko MATSUMOTO[1], Kazuhiro HAGINOYA[1], Mamiko ISHITOBI[1], Naomi HINO-FUKUYO[1], Noriko TOGASHI[1], Hiroyuki YOKOYAMA[1], Mitsutoshi MUNAKATA[1], Kazuie IINUMA[2]
([1]Sendai, [2]Ishinomaki, Japan)

POSTER 19 10th ISS

Neuroepidemiology of West syndrome and early infantile epileptic encephalopathy in Miyagi prefecture, Japan

Naomi HINO-FUKUYO[1], Kazuhiro HAGINOYA[1], Kazuie IINUMA[2], Shigeru TSUCHIYA[1]
([1]Sendai, [2]Ishinomaki, Japan)

POSTER 20 10th ISS

Early onset is a risk factor of unfavorable prognosis of myoclonic-astatic epilepsy

Takahito INOUE[1], Yukiko IHARA[1], Yuko TOMONO[1], Sawa YASUMOTO[1], Atsushi OGAWA[1], Masaharu OHFU[1], Akihisa MITSUDOME[2], Shinichi HIROSE[1]
([1,2]Fukuoka, Japan)

POSTER 21 10th ISS

Developmental delay, epilepsy, and neonatal diabetes (DEND) syndrome: early diagnosis and oral sulfonylurea therapy potentially improve neurodevelopment

Akiko UEHARA[1], Ayako SOFUE[1], Tatsuya FUKASAWA[1], Makoto MORITA[1], Shinji HASEGAWA[1], Kazuyoshi WATANABE[1], Jun NATSUME[2]
([1,2]Nagoya, Japan)

POSTER 22 10th ISS

Clinical and electrophysiological characteristics of infantile spasms observed in children in the Republic of Kazakhstan (infantile spasms, dysgenesis of brain, intrauterine infection, perinatal encephalopathy, tuberous sclerosis)

M. LEPESSOVA, B. MYRZALIYEVA, Z. MEDETBEKOWA, G. TAIROVA
(Almaty, Republic of Kazakhstan)

POSTER 23 10th ISS

Epilepsy presenting as major manifestation of primary brain tumor in children

Ching-Wan TSAI, Kun-Long HUNG
(Taipei, Taiwan)

Poster Visit
Day 2

NEUROIMAGING

POSTER 24 10th ISS

Diffusion weighted image abnormalities and glucose hypometabolism in patients with prolonged febrile seizures

Jun NATSUME[1,3], Neda BERNASCONI[2], Megumi MIYAUCHI[1], Misako NAIKI[1], Taro YOKOTSUKA[1], Koichi MARUYAMA[3], Ayako SOFUE[1], Andrea BERNASCONI[2]
([1,3]Nagoya, Japan, [2]Montreal, Canada)

POSTER 25 10th ISS

FDG-PET study of patients with genetically confirmed patients with severe myoclonic epilepsy in infancy

Kazuhiro HAGINOYA[1], Noriko TOGASHI[1], Taro KITAMURA[1], Mitsugu UEMATSU[1], Tomoko KOBAYASHI[1], Yoko MASTSUMOTO[1], Yosuke KAKISAKA[1], Keisuke WAKUSAWA[1], Naomi HINO-FUKUYO[1], Mamiko ISHITOBI[1], Kazuie IINUMA[2], Shigeru TSUCHIYA[1], Tomohiro KANETA[3], Kazuhiro YAMAKAWA[4]
([1,3]Sendai, [2]Ishinomaki, [4]Saitama, Japan)

POSTER 26 10th ISS

Activation of subcortical gray matter during spasms in patients with West syndrome: subtraction SPECT

Yosuke KAKISAKA[1], Kazuhiro HAGINOYA[1], Mamiko ISHITOBI[1], Noriko TOGASHI[1], Taro KITAMURA[1], Keisuke WAKUSAWA[1], Ikuko SATO[1], Naomi HINO-FUKUYO[1], Mitsutoshi MUNAKATA[1], Hiroyuki YOKOYAMA[1], Kazuie IINUMA[1], Tomohiro KANETA[2], Shigeru TSUCHIYA[1]
([1,2]Sendai, Japan)

POSTER 27 10th ISS

Characteristics of SPECT and PET of brain in severe myoclonic epilepsy: a case report

Shyi-jou CHEN[1], Kai-ping CHANG[2], Chin-chin WANG[1]
([1,2]Taipei, Taiwan)

ABSTRACTS
(Oral Presentation)

INVITED

MOLECULAR PATHOGENESES OF EPILEPSY RESULTING FROM CHANNEL DYSFUNCTION

ORAL 1 10th ISS

Shinichi HIROSE

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

Mutations of genes encoding ion channels were found in several epilepsy syndromes. Dysfunctions of channels resulting from the mutations have been demonstrated in vitro. The notion that certain types of epilepsy are diseases of channels or channelopathy seems to be legitimate and facilitates our understanding of molecular pathogenesis of epilepsy. For example, in benign familial neonatal convulsions (BFNC), an autosomal dominant epilepsy phenotype which afflicts only neonates, heterozygous mutations of the genes encoding subunits of KCNQ K+ channels, KCNQ2 and 3, were identified. The mutations have been found to impair K+ currents called M-current. M-current is believed to control subthreshold neuronal excitability and thus its impairments can cause convulsions. Autosomal inheritance of BFNC is explained by the fact that heterozygous mutations lead haploinsufficiency and the age dependency may be associated with the developments of ion channels. Thus, in the brain of neonates where KCNQ2 and 3 are coexpressed, KCNQ K+ channels serve as the major inhibitory system before GABAA receptor exerts inhibitory function. Furthermore, mutations of Na+ channels and GABAA receptors identified in sever myoclonic epilepsy in infancy have extended the concept of channelopathy in epilepsy. Thus, new pathomechanisms of channelopathy such as intracellular trafficking defect of channels, parental mosaicism and micro deletions have been disclosed. However, such dysfunctions of channels do not necessarily illustrate epilepsy phenotypes and studies with genetic engineered model animals are required to bridge the gap.

INVITED

ORAL 2 10th ISS

FUNCTINAL EFFECTS OF SODIUM CHANNEL MUTATIONS THAT CAUSE GEFS+

Alan L. GOLDIN[1], Karoni DUTT[1], Arthur J. BARELA[1], Jay SPAMPANATO[1,3], Bin TANG[2], Andrew ESCAYG[2]

[1]Departments of Microbiology & Molecular Genetics and Anatomy & Neurobiology, University of California, Irvine, CA, USA

[2]Department of Human Genetics, Emory University, Atlanta, GA, USA

[3]Current Address: Department of Neurology, David Geffen School of Medicine, UCLA, Los Angeles, CA, USA

Background: General Epilepsy with Febrile Seizures Plus (GEFS+) is an autosomal dominant familial syndrome with a complex seizure phenotype that results from mutations in one of five different ion channel subunits, three of which form part of the voltage-gated sodium channel. The majority of known GEFS+ mutations have been identified in the *SCN1A* gene encoding the sodium channel $Na_v1.1$ α subunit.

Methods: We characterized the effects of *SCN1A* mutations that cause GEFS+ by constructing each mutation in a cDNA clone encoding the orthologous rat $Na_v1.1$ sodium channel and recording the electrophysiological properties in *Xenopus* oocytes. To examine neuronal function, we used a Bacterial Artificial Chromosome to construct transgenic mice expressing the R1648H mutation and recorded sodium channel activity in dissociated cortical neurons from the mice.

Results: Each mutation altered a different aspect of sodium channel function, and the effects varied depending on the expression system. For example, the R1648H mutation accelerated recovery from inactivation in *Xenopus* oocytes but not in cortical neurons. Instead, this mutation caused a negative shift in the voltage-dependence of inactivation only in pyramidal neurons and increased use-dependence only in bipolar neurons. Both of these effects would lead to decreased sodium channel activity.

Conclusions: These results indicate that the effects of sodium channel mutations depend on the specific neurons in which the channel is expressed, which would strongly influence the GEFS+ phenotype.

Supported by NIH and the McKnight Foundation

INVITED

CLINICAL EXPRESSIONS OF ION CHANNEL EPILEPSY DISORDERS

ORAL 3 10th ISS

Alexis ARZIMANOGLOU

University Hospital Robert Debré, Department of Child Neurology & Metabolic Diseases Paris, and Institute for children and adolescents with epilepsy (IDEE), Lyon, France

The role of ion channels in epilepsy has been suspected years ago, mainly on the basis of physiology arguments: ion channels (Na+, K+) are responsible for the genesis of action potentials, neurotransmitter receptors are themselves channels or coupled to ion channels and a number of currently used anti-seizure drugs directly or indirectly influence their function. Recent data from molecular genetics confirmed the implication of ion channels in the genesis of epilepsy seizures. Ion channels are distributed differently in different parts of the neuron, probably allowing specific excitability profiles. Ion channel expression and distribution also varies as a function of development.

Since the first voltage-gated ion channel defect in human epilepsy was reported, involving a potassium channel defect mutation that caused one of the most benign types of epilepsy, *benign familial neonatal convulsions*, more than 10 mutated genes have been identified. They code for sodium or chloride channel subunits as well as neurotransmitter receptor subunits. The epilepsy syndromes related to these genes reflect a spectrum of clinical severity. This is true not only for syndromes related to different ion channels (*benign familial neonatal convulsions as opposed to Dravet syndrome*) but also for syndromes found in members of families with a sodium channel defect (*the spectrum of phenotypes in families described as GEFS plus*). Great individual variations in the presentation and prognosis have been described within members of families with the same epilepsy syndrome (*ADNFLE*). Despite the difficulties to correlate phenotypes and genotypes, suggesting diverse pathophysiological mechanisms, current advances of our understanding will make possible the discovery of new and better-targeted therapies, including preventive ones.

ORAL
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10th ISS

RISK FACTORS FOR POSTNEONATAL EPILEPTIC SEIZURE IN THE NEWBORNS WITH NEONATAL SEIZURES

Hiroshi OTSUBO, Sang-Ook NAM, Ayako OCHI, O. Carter SNEAD III

Division of Neurology, The Hospital For Sick Children, Toronto, Ontario, Canada

Background: To determine the risk factors for postneonatal epileptic seizure in the newborns who have neonatal seizures confirmed by EEG.

Methods: We retrospectively examined 35 infants who had neonatal seizures confirmed by EEG recorded between February 1999 and September 2001 at the Hospital for Sick Children, and had follow up for at least 18 months. We divided these infants into two groups; group A with postneonatal epileptic seizure and group B without postneonatal epileptic seizure. EEG was digitally recorded with 13 electrodes. EEG seizure was defined as a burst of paroxysmal or repetitive electrical activities that sustained at least 10 seconds in duration.

Results: Postneonatal epileptic seizure developed in 15 patients (43%, group A) and no postneonatal epileptic seizure developed in 20 patients (57%, group B). Conceptional age at EEG seizures was older in group A (42.0 ± 4.4 weeks) than that of group B (39.4 ± 3.7 week) (P = 0.0369). Abnormal EEG background activity occurred in group A (10/15, 67%) more often than in group B (7/20, 35%) with a tendency (P = 0.0636). The duration of EEG seizure tended to be longer in group A (124 ± 224 seconds) than in group B (42 ± 52 seconds) (P=0.0634).

Conclusion: Our results suggest that older conceptional age at neonatal seizure, abnormal EEG background activity and the longer duration of EEG seizure predict postneonatal epileptic seizures.

INVITED

RECENT ADVANCES IN THE TREATMENT OF NEONATAL SEIURES

ORAL 5 10th ISS

Kevin J. STALEY

Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

High expression levels of the Na^+–K^+–$2Cl^-$ (NKCC1) co-transporter in immature neurons lead to an increase in intracellular chloride ions and a depolarized Cl^- equilibrium potential (E_{Cl}). This results in efflux of Cl^- through open $GABA_A$ channels. This is the opposite of what occurs in mature neurons, in which $GABA_A$ receptor activation is inhibitory. This reversed Cl- flow excites the neurons, lowers the seizure threshold, and explains why the EEG response to anticonvulsants such as barbiturates and benzodiazepines that prolong the opening of GABA channels. Because the maturation of neuronal chloride transport occurs in a caudal-rostral direction, the spinal cord and brainstem have mature, inhibitory responses to GABA and the respond appropriately to anticonvulsants that work on the GABA channel. This may explain why the EEG demonstrates that seizure activity in the newborn cortex is not reduced by GABAergic anticonvulsants, although the clinical expression of the seizures is reduced, most probably at the level of the brainstem and spinal cord. Blocking the NKCC1 transporter with bumetanide prevents reversed Cl^- flux in immature neurons and reduces EEG seizure activity in the immature brain. Because bumetanide changes the driving force for Cl efflux, Ohm's law indicates that the bumetanide anticonvulsant effect should be multiplicative, not additive, with anticonvulsants that increase the GABA conductance. Phenobarbital in combination with bumetanide abolished seizures in 70% of preparations and significantly reduced the frequency, duration and power of seizures in the remaining 30%; this was far better than either drug alone. Thus, the combination of these bumetanide and Phenobarbital may comprise an effective therapy for early-life seizures.

INVITED

ORAL 6 10th ISS

THE VULNERABILITY OF HIPPOCAMPAL NEURONS TO INFANTILE SEIZURES

John W. SWANN

The Cain Foundation Laboratories, Baylor College of Medicine, Houston, Texas, USA

The impact recurrent seizures have on the developing brain remains controversial. However recent clinical observations suggest that cognitive disabilities are more likely to accompany intractable epilepsy in children than in adults - leading some to propose that the developing brain may be uniquely vulnerable in this regard. Indeed, it is well documented from animal models that brief, recurrent seizures in infancy can produce long-term cognitive deficits. A number of laboratories have set out to understand the underlying cellular and molecular mechanisms. Results have shown that neuronal cell death does not occur in these animals. However, dendritic abnormalities in hippocampal pyramidal cells have been reported. These consist of decreases in dendritic branching and spine density. These results have been supported by recent molecular studies where decreases in the expression of postsynaptic and dendritic cytoskeletal proteins are observed in several animal models of early-onset epilepsy. Recent results from a new in vitro model suggest that epileptiform activity suppresses the growth of immature hippocampal pyramidal cell dendrites. Molecular events that may underlie this suppression of growth will be discussed since these are potential targets for new therapies that would be aimed at limiting the cognitive deficits that occur in children with intractable seizure disorders.

GENETIC SUSCEPTIBILITY TO FEBRILE SEIZURES; INTERLEUKIN-10 ATTENUATES FEBRILE SEIZURE SUSCEPTIBILITY

ORAL 7 10th ISS

Yoshito ISHIZAKI[1], Ryutaro KIRA[1], Mitsumasa FUKUDA[2], Hiroyuki TORISU[1], Masafumi SANEFUJI[1], Naoko YUKAYA[1], Mariko IWAYAMA[1], Toshiro HARA[1]

[1]Department of Pediatrics, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
[2]Department of Pediatrics, Ehime University School of Medicine, Ehime, Japan

Background: Febrile seizures (FS) are the most common form of childhood convulsions. Genetic factors are known to play an important role in susceptibility to FS. We previously reported that interleukin-1 beta (IL1B) -511T allele was associated with susceptibility to simple FS of sporadic occurrence (Kira, 2005). Here, we investigated whether other inflammatory cytokine genes contributed to the development of FS. In addition, we studied the role of IL-10 in hyperthermia-induced seizures in developing rats.

Methods: Five functional single nucleotide polymorphisms (SNPs) of four inflammatory cytokine genes (TNFA -1037C/T, IL6 -572C/G, IL8 -251A/T, IL10 -1082A/G and -592A/C) were assessed in 249 FS patients (186 simple and 63 complex FS) and 225 controls. SNPs were genotyped by a TaqMan platform. Haplotype analyses were performed for the two IL10 SNPs tested. We applied human recombinant IL-10 and saline intra-nasally to developing rats (each 8 male Lewis rats, 20-24 days-old) 1h before seizures induced by moist heated air.

Results: The frequencies of IL10 -592C allele and IL10 -1082A -592C haplotype were significantly less in FS than controls ($p=0.013$, $p=0.014$, respectively). The seizure threshold temperature of IL-10 group was significantly higher than controls ($p=0.027$).

Conclusions: IL10 -592C allele and IL10 -1082A -592C haplotype, which associated with higher production, contributed to the genetic resistance to FS. IL-10 had an anti-convulsant effect in hyperthermia-induced seizures. Thus, IL-10 might attenuate FS susceptibility by increased seizure thresholds.

ORAL
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10th ISS

ARX MUTATION IN FEMALES; AN UNDER-RECOGNIZED CAUSE OF EPILEPSY AND DEVELOPMENTAL DELAY

Amanda W. PONG, Yaman Z. EKSIOGLU, Masanori TAKEOKA

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

Background: *ARX* is an X-linked *Aristaless*-related homeobox gene important for differentiation and migration of GABAergic interneurons from ganglionic eminence to neocortex and hippocampus. Males present with epilepsy, developmental delay, micropenis, dystonia, or autism. Females have rarely been discovered as a consequence of *ARX* mutations in male relatives.

Methods: We identified three females with *ARX* mutations at Children's Hospital Boston, with mental retardation, epilepsy and psychiatric disease. *ARX* mutation analysis was performed by the Clinical Molecular Diagnostic Laboratory at City of Hope National Medical Center, Duarte, CA.

Results: Case 1: 12 year-old girl with mental retardation and anxiety. Mutation analysis reveals heterozygous deletion of 6 base pairs at nucleotide 330 in exon 2, with compression of polyalanine tract.

Case 2: 7 month-old girl with infantile spasms and developmental regression. Mutation analysis reveals heterozygous deletion of 24 base pairs at nucleotides 441-464 in exon 2, with compression of polyalanine tract.

Case 3: 29 year-old woman with developmental delay and anxiety, mother of male infant with Ohtahara syndrome. Mutation analysis reveals heterozygous 1 base pair insertion C at nucleotides 1471-1472 in exon 5 causing frameshift.

Conclusions: We report three novel heterozygous *ARX* mutations in females with mental retardation, psychiatric disease and infantile spasms. Testing for *ARX* mutations should be considered in females with epilepsy and developmental delay, even with no family history, especially when investigations for common structural and genetic causes are unrevealing.

A LONGER POLYALANINE EXPANSION MUTATION IN THE ARX GENE CAUSES OHTAHARA SYNDROME

ORAL 9 10th ISS

Mitsuhiro KATO[1], Shinji SAITOH[2], Atsushi KAMEI[3], Hideaki SHIRAISHI[2], Yuki UEDA[2], Manami AKASAKA[3], Jun TOHYAMA[4], Noriyuki AKASAKA[4], Kiyoshi HAYASAKA[1]

[1]Pediatrics, Yamagata University School of Medicine, Yamagata, Japan
[2]Pediatrics, Hokkaido University Graduate School of Medicine, Sapporo, Japan
[3]Pediatrics, Iwate Medical University, Morioka, Japan
[4]Pediatrics, Nishi-Niigata Chuo National Hospital, Niigata, Japan

Background: Ohtahara syndrome (OS) is one of the most severe and earliest forms of epilepsy and often evolves to West syndrome (WS). The pathogenesis of OS remains unclear. ARX is a crucial gene for the development of interneurons in the fetal brain and polyalanine expansion mutations of ARX cause mental retardation or seizures including WS in male. We aimed to reveal the contribution of ARX in the pathogenesis of OS.

Methods: Blood samples were collected from three sporadic male patients with OS with the informed consent from their guardians. All patients showed a transition from OS to WS after several months. Genomic DNA was extracted and the ARX gene was analyzed by denaturing high performance liquid chromatography and direct sequencing.

Results: A hemizygous de novo 33 bp-duplication in exon 2, 298_330dupGCGGCA(GCG)9, which is thought to expand the original 16 alanine residues to 27 alanine residues (A110_A111insAAAAAAAAAAA) in the first polyalanine tract of the ARX protein, was found in two unrelated patients.

Conclusions: Although OS is mainly associated with brain malformations, ARX is the first responsible gene for idiopathic OS. The size of polyalanine expansions correlates with the severity of clinical phenotypes and abnormal aggregation in transfected cells. Our observation that OS had longer polyalanine expansion than WS is consistent with the findings of earlier onset and more severe phenotypes in OS than in WS.

ORAL 10 10th ISS

DISTINCT CLINICAL COURSE OF SMEI WITH SCN2A MUTATION - COMPARISON WITH SCN1A MUTATIONS

Hitoshi OSAKA[1], Emi MAZAKI[2], Nami OKAMURA[2], Sumimasa YAMASHITA[1], Mizue IAI[1], Michiko YAMADA[1], Kazuhiro YAMAKAWA[2]

[1]Division of Neurology, Kanagawa Children's Medical Center, Yokohama, Japan
[2]Laboratory for Neurogenetics, RIKEN Brain Science Institute, Wako, Japan

Background: Two neuronal voltage-gated sodium channel (SCN) alpha 1 subunit, SCN1A, and alpha 2 subunit, SNC2A, are very similar at the amino acid level (identical at 88%). These two channels have non-overlapping subcellular distributions and the different temporal expression. Role of SCN 2A on fever sensitive epilepsy remains unclear as a paucity of reported cases. We present one case with severe myoclonic epilepsy (SMEI) carrying a novel SCN2A mutation (F328V) and compare the phenotype with our nine SMEI cases carrying SCN1A mutations.

Clinical Details: A 4-year-old girl exhibited febrile generalized tonic-clonic convulsion lasting 30 min at 1 years and 3 months. Within 2 weeks, she exhibited afebrile myoclonic, absence seizures more than ten times a day, followed by generalized or unilateral tonic-clonic convulsions few times a day. Valproic acid was initiated and partially effective for these convulsions. At 18 months, she showed frequent seizures during bathing, some of which lasted more than 30 min. She was ataxic, mildly delayed for motor development and diagnosed as SMEI. Although seizures continued for a year despite of sodium bromide and clonazepam, they ceased when she was 3-years of age without any changes of anti-epileptic drugs. Now, she is seizure free for more than 6 months and shows no developmental delay.

Conclusions: This case with SCN 2A mutation showed a rapid resolution of frequent, various type of seizures, which sharply contrasts to our SMEI patients with SCN1A mutations.

INVITED

FACTORS INFLUENCING THE CHOICE OF TREATMENTS IN EPILEPSY

ORAL 11 10th ISS

Solomon L. MOSHÉ

Neuroscience and Pediatrics, Albert Einstein College of Medicine, Bronx, New York, USA

Although there are many common mechanisms involved in the generation of seizures, there are several factors that influence the choice of medication to be initiated or maintained. In this presentation, older and newer antiepileptic drugs (AEDs) will be discussed in terms of bioavailability and side effect profiles. The goal is to provide helpful points that may aid clinicians on how to choose AEDs for specific syndromes as a function of age, including treatments of syndromes that are intractable to current antiepileptic treatments. Nevertheless, there is an urgent need to develop neuroprotective strategies to influence the long term outcome. The choice of AEDs should take into account the putative neuroprotective effects these drugs may have. Alternatively rational polypharmacy can be considered to address both seizure control and neuroprotection as a function of age.

INVITED

ORAL 12 10th ISS

LINKING BIOCHEMICAL PATHWAYS AND SEIZURE SUSCEPTIBILITY IN EARLY LIFE: LESSONS FROM INBORN ERRORS OF METABOLISM.

Asuri PRASAD[1], Chitra PRASAD[2]

[1]Department of Pediatrics and Clinical Neurosciences,

[2]Section of Genetics and Metabolism, Department of Pediatrics, Schulich School of Medicine and Dentistry, University of Western Ontario, London, Ontario, Canada

Background: Seizure susceptibility in early life can be traced to age dependent changes occurring at multiple levels of nervous system structure and function. Inborn errors of metabolism, though rare, often present as epileptic encephalopathies in infancy.

Methods and Results: A Medline search was carried out using the following terms "epileptic encephalopathy" AND "inborn errors of metabolism" yielded 132 publications. Of these, 63 case reports met the selection criteria (All Infant: birth-23 months, published in the last 10 years, Case Reports). These could be grouped in the following categories; acute toxic encephalopathies, disorders of purine & pyrimidine biosynthesis, energy metabolism, neurotransmitter biosynthesis and metabolism. Other categories included; vitamin responsive seizures, abnormalities of calcium metabolism, and subcellular organelle dysfunction (mitochondria, peroxisomes, and lysosomes). A few of these inherited disorders present with distinct electroclinical syndromes, while a majority present with mixed seizures and non specific features. Widespread energy deficits, accumulation of neurotoxic precursors, disturbances in cerebral development and neuronal migration, induction of acute cerebral insults, shifts in the balance between excitation and inhibition, are putative mechanisms through which genetic aberrations in biochemical pathways induce long term alterations in neuronal excitability.

Conclusions: Infantile epilepsies associated with inborn errors of metabolism provide fresh insights into mechanisms of seizure susceptibility in the developing brain. Treatments capable of modifying the natural history of these disorders can be developed based on a better understanding of the underlying mechanisms.

INVITED

GENDER INFLUENCES ON THE MATURATION OF ENDOGENOUS SYSTEMS INVOLVED IN SEIZURE CONTROL

ORAL 13 10th ISS

S. L. MOSHÉ

Neuroscience and Pediatrics, Albert Einstein College of Medicine, Bronx, New York, USA

The immature brain is more susceptible to the development of seizures and status epilepticus (SE) than the mature brain. The increased susceptibility may be related to age- and sex-specific patterns in the functionality of neuronal networks involved in seizure control. The substantia nigra pars reticulata (SNR) is one of the brain sites critically involved in cognition, motor behaviors and control of seizures. In the SNR there are two topographically discrete regions ($SNR_{anterior}$ and $SNR_{posterior}$) with specific GABAergic features. These two regions mediate distinct effects on seizures using divergent output networks in response to localized infusions of $GABA_A$ agents. The SNR based systems are developmentally regulated and have sexually dimorphic features in terms of their ability to influence the expression of generalized clonic seizures. Genetic and epigenetic factors are responsible for the maturation of SNR function. Deviation from normal developmental process may have profound influences on long-term outcomes on seizure control with age and on cognitive disorders as autism. For example, SE during critical periods of development may distort GABA based functions of the SNR. These alterations must be taken into account to identify novel age- and possibly sex-specific neuroprotective / disease modifying agents that can be used to prevent or restore some of the detrimental effects of SE early in life on SNR, a structure with widespread influences on brain function in health and disease.

INVITED

ORAL 14 10th ISS

HOW STRESS EARLY IN LIFE ENHANCES SEIZURE SUSCEPTIBILITY

Tallie Z. BARAM

Departments of Pediatrics, Anatomy & Neurobiology, Neurology; University of California, Irvine, CA, USA

Seizures often arise in the setting of acute injury or insult. In addition, many epilepsies are "symptomatic", occurring late after infection, trauma, or stroke. The mechanisms by which these diverse factors provoke both acute seizures and epilepsy are not fully understood. Each of these insults may initiate a unique chain of events that promotes epilepsy; alternatively, all may share commonalities that initiate cellular and molecular changes that promote neuronal hyperexcitability. For example, epilepsy- provoking insults are stressful, in that they trigger the release of 'stress-mediating molecules', including glucocorticoids and the neuropeptide corticotropin releasing hormone (CRH). Stress induces release of CRH from hippocampal interneurons, and CRH acts on selective receptors (CRFR1) to enhance glutamate-mediated neurotransmission. In immature hippocampus, CRH and its receptors are particularly abundant, and the peptide may excite neurons sufficiently to evoke seizures, followed by dendritic atrophy or death of vulnerable neurons. In animal models, chronic enhancement of hippocampal CRH levels may provoke enduring reduction of hippocampus-governed learning and memory. In humans, high CRH levels are found in infants with chronic CNS stressors including congenital infection, dysplasia, trauma or recurrent seizures. Drugs that reduce CRH levels in limbic structures (e.g., ACTH) are potent antiepileptics in the developing CNS. In summary, acute and chronic stress releases CRH, promoting seizures. The seizures further activate the ''stress response'', leading to a vicious cycle culminating in loss of neuronal function and integrity.

INVITED

HOW NURTURE SHAPES NATURE: THE ROLE OF THE ENVIRONMENT ON THE DEVELOPMENT OF SEIZURE ACTIVITY

ORAL 15 10th ISS

Ulrich SCHRIDDE[1,2], Gilles VAN LUIJTELAAR [2]

[1]Department of Neurology, Yale University School of Medicine, New Haven, USA

[2]Department of Biological Psychology, Radboud University Nijmegen, Nijmegen, The Netherlands

Background: Although childhood absence epilepsy has a genetic origin, evidence suggests that environmental factors also influence the final phenotypic expression of the disease. Our aim was to find out in how far and in which way genotypic and environmental influences during development affect the phenotypic expression of the seizures.

Methods: Inbred rat strains that differed in genetic seizure susceptibility (epileptic WAG/Rij & ACI, nearly seizure free) underwent various environmental manipulations during different stages of development and influences of strain and environment on seizures activity were investigated. For early environmental manipulations we also investigated if alterations in seizure activity are correlated with changes in hyperpolarization activated cation channels (HCN).

Results: We found that while the occurrence of seizures has a strong genetic component, seizure characteristics like number and mean duration have different heritabilities and are sensitive to environmental influences throughout life; though they differ in their sensitivity. The latter possibly depends on the type of environmental manipulation, its timing, or both. Furthermore, we found that changes in seizure activity after early environmental manipulations are accompanied by changes in cortical HCN.

Conclusion: Genetically determined absence seizures are quite sensitive for environmental manipulations, especially early in life. The environmental effects on absence epilepsy are rather complex and caused by a combination of factors. We propose that the environment influences seizures via various seizure mediating mechanisms, and that ion channels like HCN might be involved.

INVITED

ORAL 16 10th ISS

GENETIC MALFORMATIONS OF THE CEREBRAL CORTEX AND SEIZURE SUSCEPTIBILITY DURING INFANCY

Ganeshwaran H. MOCHIDA

Department of Neurology, Beth Israel Deaconess Medical Center, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, USA

Genetic malformations of the cerebral cortex are an important cause of epilepsy in children. Each genetic malformation has unique characteristics in terms of epileptogenicity, age of seizure onset, and types of seizure. Therefore, finding the genetic causes for these disorders is expected to lead to a better understanding of the biological mechanisms of epilepsy. Microcephaly vera (MV) is a genetically heterogeneous disorder that affects proliferation of neuronal progenitor cells, and shows a very low incidence of epilepsy. However, recently we reported a family with a mutation in ASPM (the most common causative gene for MV) with severe seizures, expanding the clinical spectrum of the disorder. Disorders that affect neuronal migration and organization of the cerebral cortical layers, including lissencephaly, polymicrogyria, and schizencephaly, on the other hand, are generally highly epileptogenic. Recently several familial cases of schizencephaly and unilateral polymicrogyria were reported, and are being studied for their underlying genetic defects. Disorders that affect the integrity of the pial surface (cobblestone dysplasia or type II lissencephaly), are also highly epileptogenic. One of the disorders associated with cobblestone dysplasia, Walker-Warburg syndrome (WWS), has been found to be genetically highly heterogeneous. Though mutations in POMT1 account for some cases of WWS, a large number of patients do not have a mutation in the gene, suggesting the presence of additional causative genes.

INVITED

FETAL SYNAPTOGENESIS AND INFANTILE EPILEPSIES

ORAL 17 10th ISS

Harvey B. SARNAT, Laura FLORES-SARNAT

Pediatrics, Pathology (Neuropathology) and Clinical Neuroscience, University of Calgary, Faculty of Medicine, Calgary, Alberta, Canada

Introduction: Synaptogenesis is an important late developmental process in the ontogeny of the brain. There is no means of demonstrating it by functional imaging or magnetoencephalography. EEG shows large fields of cortical electrical activity and the maturation of the EEG in preterm infants reflects synaptogenesis indirectly. In sections of fetal brain tissue at autopsy, synapses may be demonstrated by synaptophysin, an immunocytochemical marker of a structural protein of the synaptic vesicle wall.

Materials and Methods: Over a 28-month period, 153 human fetal and neonatal brains were studied to survey spatial and temporal sequences of synaptophysin reactivity in various regions. Fetuses ranged from 6- 41 wk postconception age. Exclusion criteria were chromosomopathies, major malformations, chronic metabolic or hypoxic/ischaemic encephalopathy, massive hydrocephalus and ventriculitis. In relation to epilepsy, this report focuses on 1) brainstem tegmentum and reticular formation; 2) basal ganglia; 3) hippocampus; 4) cerebral neocortex. Macerated brains of 12 stillborns of various ages, with extensive autolytic change, were studied separately.

Results: 1) The tegmentum, including parts of the reticular activating system, peri-aqueductal grey matter and raphé nuclei, begins showing synaptophysin reactivity as early as 9 weeks gestation, and is complete by 15 weeks. 2) The caudate nucleus and putamen show a patchy, striated pattern of strong reactivity alternating with no reactivity beginning at 13 weeks and not complete until near-term. These stria correspond to the "striosomes of Graybiel" of neurotransmitter-rich / neuropeptide-poor zones not seen with histological stains; 3) though the dentate gyrus forms sooner than Ammon´s horn, it does not develop synaptic activity until after 21 weeks, whereas the CA2 sector has synaptic reactivity at 14 weeks, followed by CA3, then CA4, and finally CA1 at near-term; 4) the neocortex exhibits reactivity earliest in ascending thalamocortical axons at 24-28 weeks, then surrounds neurons in deep layers at 30 weeks, followed by the middle layers and finally layer 2 at near-term. Synanptophysin is a robust molecule that resists postmortem autolysis for as long as 48 hours, hence is reliable for studying stillborns.

Comment: Correlations with clinical neurological examination and EEG maturation of preterm neonates can be made with the sequence of synaptogenesis here shown. Synaptophysin also correlates with other markers of neuronal maturation. Some regions, such as the thalamus and amygdala, remain incompletely studied. These normal data provide a basis for the analysis of synaptogenesis in cerebral malformations. Preliminary results already indicate abnormal synaptic distributions and timing in cerebral dysgeneses and may help explain some neonatal and infantile epilepsies.

INVITED

ORAL 18 10th ISS

SEIZURE SUSCEPTIBILITY IN TUBEROUS SCLEROSIS COMPLEX: MOLECULAR PATHOGENESIS AND RATIONALE FOR TREATMENT

Paolo CURATOLO

Pediatric Neurology Unit, Department of Neuroscience, Tor Vergata University, Rome, Italy

Tuberous Sclerosis Complex (TSC) is an autosomal dominant disorder affecting 1 in 6000 individuals. Nearly 90% of TSC patients experience epilepsy, and in many cases seizures are unresponsive to AEDs. The majority of children with TSC have onset of seizures during the first year of life, and up to one-third of them will develop infantile spasms. Seizures have a focal or multifocal origin with a topographic correspondence between EEG foci and MRI lesions, demonstrating the preponderal role of cortical tubers as epileptogenic foci. However, non-tuberous brain regions, characterized by disorganized cortical lamination and dysplastic neurons with aberrant dendritic arbors or axonal projections play a critical role in generation of abnormal electrical activity. Resected tuber tissue and its immediately adjacent cortex demonstrates abnormal excitatory pathways and disturbance of the GABA-mediated synaptic inhibition. Recent evidence shows that loss of TSC1 or TSC2 triggers enlargement of somas and dendritic spines, and alters the properties of glutamatergic synapses in neurons. Furthermore, inhibitory cortical GABAergic interneurons are altered in the cortical tubers of TSC children.

Epileptogenesis in TSC may be caused by the imbalance of decreased inhibition, secondary to molecular changes in GABA receptors in giant cells and dysplastic neurons, and increased excitation, secondary to molecular changes of glutamate receptors in dysplastic neurons. The deficiency of GABAergic interneurons may explain the early onset and severity of seizures in TSC. In conclusion, epilepsy in TSC seems to arise from the complex interaction between multiple areas, all of which have increased excitability and reduced inhibition.

EVOLUTION OF EEG IN YOUNG INFANTS WITH TUBEROUS SCLEROSIS. CAN WE PREDICT EPILEPSY?

ORAL 19 10th ISS

Sergiusz JOZWIAK[1], Dorota DOMANSKA-PAKIEŁA[1],
Joanna SZYMKIEWICZ-DANGEL[2], Jolanta KASPRZYK-OBARA[1]

[1]Department of Neurology and Epileptology, The Children's Memorial Health Institute, Warsaw, Poland
[2]2nd Department of Obstetrics and Gynecology, Medical University in Warsaw, Poland

Background: Epilepsy appears in 70-80% of patients with tuberous sclerosis complex (TSC). Infantile spasms are the most frequent type of epilepsy. Early onset of seizures and their drug-resistance are associated with frequent mental retardation of the patients. Usually, EEG recordings are performed after seizure onset. We speculate whether EEG examination in young infants without epilepsy may help to predict seizures.
Methods: Five patients with prenatally diagnosed multiple cardiac tumors were prospectively followed-up. They were all diagnosed as having TSC. Although initially none of them presented with seizures, sleep EEG was performed in all patients.
Results: Three children developed seizures later on and two are still seizure-free. In two seizure free children both initial and follow-up EEG were normal. In other patients, the onset of seizures was preceded by abnormal EEG patterns.
Conclusions: Our results suggest that EEG abnormalities can predict epilepsy onset in TSC patients. These observations raise a question whether in such cases a "prophylactic" antiepileptic treatment is justified. On the other hand, normal EEG may serve as a good prognostic factor for normal development and seizure-freedom in TSC patients.

ABSTRACTS
(Poster Presentation)

GABA PROMOTES THE DIFFERENTIATION OF NEWBORN DENTATE GRANULE CELLS

POSTER 1 10th ISS

Junya ICHIKAWA, Yuji IKEGAYA, Norio MATSUKI, Ryuta KOYAMA

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

Background: Newborn granule cells (GCs) migrate from the tertiary dentate matrix (tdm) of dentate hilus to the granule cell layer in the early postnatal hippocampus. We presumed that the neurotransmitter GABA regulates the differentiation of newborn GCs in neonates because abundant GABAergic neurons exist in tdm. Especially in case of early-life seizure that arises from the hippocampus, tdm would be filled with GABA released from inhibitory interneurons and the GCs in the granule cell layer. Here we examined how GABA affects the differentiation of newborn GCs.

Methods: Hilar slices including tdm obtained from postnatal six-day-old (P6) rats were dissociated to prepare immature GCs. They were cultured in the presence or absence of 1 mM GABA.

Results: After four days in vitro, cultured GCs were divided to three types depending on their developmental stages: Type A, a cell with a single leading process from the spindle-shaped somata; Type B, a cell with multiple neurites; Type C, a cell with a single tau-1-positive axon and multiple MAP-2-positive dendrites. Chronic GABA application shifted the developmental stage toward Type C.

Conclusions: These results indicated that GABA facilitate the maturation of newborn GCs and may induce an emergence of mature ectopic GCs in temporal lobe epilepsy.

EFFECTS OF THE KETOGENIC DIET ON THE BRAIN-DERIVED NEUROTROPHIC FACTOR EXPRESSION AFTER KAINIC ACID-INDUCED SEIZURES IN YOUNG MICE

POSTER 2 10th ISS

Ho Jin PARK[1], Dong Wook KIM[2]

[1]Department of Pediatrics, Eulji University Scholl of Medicine, Daejeon, Korea

[2]Department of Pediatrics, Clinical Research Center, Ilsan Paik Hospital, Inje University College of Medicine, Goyang, Korea

Background: The ketogenic diet (KD) remains a therapy in search of explanation although it is an established treatment of intractable epilepsy. Calorie restriction (CR) is known to increase brain-derived neurotrophic factor (BDNF) expression. The KD was originally devised to reproduce the biochemical changes seen upon fasting (extreme CR). This study was designed to investigate the effects of the KD on the BDNF expression after kainic acid (KA)-induced seizures in young mice.

Methods: Twenty-eight young ICR mice (P21) were equally divided into four groups: (1) seizure-free normal diet (ND) group, (2) seizure-free KD group, (3) KA-seizure ND group, and (4) KA-seizure KD group. For 4 weeks, the KD groups were fed a KD, while the ND groups were fed a standard rodent chow. Seizures were induced by intraperitoneal injection of KA (30 mg/kg) in the KA-seizure groups. The seizure-free groups were injected with equal volume of physiological saline. After then, we examined the BDNF expression affected by the KD, using immunohistochemistry, western blotting, and semi-quantitative RT-PCR.

Results: In the KA-seizure KD group, immunoreactive BDNF expression was visualized outstandingly compared with other groups. Furthermore, a remarkable increase of BDNF protein and mRNA expression was observed in the hippocampus of the KA-seizure KD group in comparison with other groups.

Conclusions: Our results suggest that the KD may enhance the BDNF expression after KA-induced seizures in young mice, similar to the effects of CR.

POSTER 3 10th ISS

EARLY-LIFE SEIZURE INDUCES AN EMERGENCE OF ECTOPIC GRANULE CELLS IN ADULT MICE DENTATE GYRUS

Rieko MURAMATSU, Yuji IKEGAYA, Norio MATSUKI, Ryuta KOYAMA

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

Background: Dentate granule cells (GCs) are densely packed in the granule cell layer, but in tissues from patients or animal models of temporal lobe epilepsy, a number of mature GCs are found in abnormal areas, including dentate hilus. Such 'ectopic' GCs have been shown to contribute to the hyperexcitability of the hippocampus. Here we investigated whether seizures in early postnatal days, when most GCs are born and migrate from the hilus to the granule cell layer, induce ectopic GCs in the adult dentate gyrus.

Methods: For this purpose, we subcutaneously injected bromodeoxyuridine (BrdU) daily to postnatal zero-day-old (P0) C57BL/6 mice for three consecutive days (P0/1/2) to label dividing cells and induced seizures at P14 by intraperitoneally injecting the muscarinic agonist pilocarpine. Six months later, hippocampal slices were prepared from the animals and immunostained with anti-BrdU antibody and an antibody against the homeobox prospero-like protein Prox1, a marker of GCs. We defined BrdU- and Prox1-double positive cells as newborn (P0/1/2-born) GCs and analyzed their localization in the dentate gyrus.

Result: There were many P0/1/2-born GCs in the hilus of the early-life seizure-experienced mice whereas no such cells were found in control.

Conclusion: The present study suggests that early-life seizures disrupted the normal migration of newborn GCs and detain them in the hilus, resulting in the emergence of ectopic GCs in the adult hippocampus.

POSTER 4 10th ISS

ALTERED DISTRIBUTION OF KCC2 IN CORTICAL DYSPLASIA IN PATIENTS WITH INTRACTABLE EPILEPSY

Mitsutoshi MUNAKATA[1], Mika WATANABE[2], Taisuke OTSUKI[3], Hideyuki NAKAMA[3], Kunimasa ARIMA[4], Masayuki ITOH[5], Junichi NABEKURA[6], Kazuie IINUMA[1], Shigeru TSUCHIYA[1]

[1]Pediatrics, Tohoku University School of Medicine, Sendai, Japan, [2]Pathology, Tohoku University Hospital, Sendai, Japan

[3]Neurosurgery and [4]Laboratory Medicine, Musashi Hospital, National Center of Neurology and Psychiatry, Tokyo, Japan

[5]Mental Retardation and Birth Defect Research, National Institute of Neuroscience, National Center of Neurology and Psychiatry, Tokyo, Japan

[6]Developmental Physiology, Division of Homeostatic Development, National Institute for Physiological Sciences, Okazaki, Japan

Background: The neuron-specific K^+-Cl^- cotransporter KCC2 plays a pivotal role in K^+ and Cl^- homeostasis in the brain, markedly affecting neuronal activity. Levels and distribution of KCC2 are altered in various pathologic conditions. However, expression of KCC2 in cortical dysplasia (CD) has not been fully examined.

Methods: The immunohistochemical expression of KCC2 in 18 CD specimens obtained during epilepsy surgery was investigated. The histopathological diagnoses were focal CD (FCD) type I (eight cases), FCD type II (six cases), and hemimegalencephaly (HME; four cases). Tissue sections were immunostained for KCC2 and compared with control sections.

Results: In the mature non-dysplastic cortex, all the layers showed diffuse neuropil staining for KCC2. The somata were stained much less, although the cytosol of subcortical ectopic neurons stained densely (intrasomatic staining). In FCD type I, the cortex showed neuropil staining for KCC2, while the somata was less strongly stained. Aberrant giant pyramidal neurons were also less stained at the soma, whereas immature neurons showed intrasomatic staining. Increased numbers of ectopic neurons with intrasomatic staining were noted in the subcortical white matter. In FCD type II, dysmorphic neurons showed dense intrasomatic staining, with reduced staining of the neighboring neuropils. Balloon cells did not stain for KCC2. Dysmorphic neurons in HME also showed intrasomatic staining.

Conclusions: Although abnormal neurons within the dysplastic tissues expressed KCC2, the subcellular distribution of KCC2 was altered differently among these neuronal populations. This might be involved in the intrinsic epileptic activity of these dysplastic tissues.

NONFUNCTIONAL SCN1A IS COMMON IN SEVERE MYOCLONIC EPILEPSY IN INFANCY

POSTER 5 10th ISS

Iori OHMORI[1], Kris M KAHLIG[2], Thomas H RHODES[2], Dao W WANG[2], Mamoru OUCHIDA[3], Hideki MATSUI[1], Alfred L GEORGE Jr[2]

[1]Department of Cellular Physiology, Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University, Okayama, Japan

[2]Division of Molecular Genetics, Department of Medicine, Vanderbilt University, Nashville, USA

[3]Department of Genetic Medicine, Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University, Okayama, Japan

Background: Mutations in SCN1A, encoding the human Na(V)1.1 neuronal voltage-gated sodium channel, cause the syndrome of severe myoclonic epilepsy of infancy (SMEI). Most SMEI-associated mutations are predicted to truncate the SCN1A protein, likely causing a loss of sodium channel function. However, many missense or in-frame deletion SCN1A mutations have also been reported in this disorder, but their functional impact is largely unknown. Here we report the functional characterization of eight SCN1A mutations previously identified in SMEI probands.

Methods: SCN1A mutants were constructed in a recombinant human SCN1A and then heterologously expressed in human HEK cells. Whole-cell patch-clamp recording was used to define biophysical properties of each mutant and for comparison with the wild-type (WT) channel.

Results: Six of the mutants were nonfunctional, but Y426N and T1909I generated measurable sodium channel activity. Cells expressing Y426N and T1909I had significantly lower current densities compared with WT-SCN1A. In addition, other biophysical abnormalities were observed for the two functional mutants including decreased channel availability (Y426N) and increased persistent sodium current (T1909I).

Conclusions: We conclude that SMEI is caused either by complete loss of SCN1A function, or by dysfunctional sodium channels exhibiting mixed biophysical properties. This wide spectrum of functional defects observed among SCN1A mutations suggests that SMEI may result from more than a single molecular or cellular mechanism, or require other factors for pathogenesis.

FREQUENCIES OF SINGLE NUCLEOTIDE POLYMORPHISMS OF THE MULTIDRUG RESISTANCE 1 GENE IN KOREAN POPULATION

POSTER 6 10th ISS

Young Ok KIM[1], Myeong Kyu KIM[2], Young Jong WOO[1], Min Cheol LEE[3], Jin Hee KIM[2]

Departments of [1]Pediatrics, [2]Neurology, and [3]Pathology, Chonnam National University Hospital, Gwangju, Korea

Background: This study compared the genetic characteristics of single nucleotide polymorphisms (SNPs) in the multidrug resistance 1 (MDR1) gene of healthy Koreans with those of other ethnic groups.

Methods: The genotype frequencies of three MDR1 SNPs (T1236C, G2677T/A, and C3435T in exons 12, 21, and 26, respectively) were determined for 115 healthy Koreans and for the members of other ethnic groups.

Results: The allele frequencies were as follows: at the 1236 site, 59% T and 41% C; at 2677, 48% G, 35% T, and 17% A; and at 3435, 65% C and 35% T. The genotype frequencies were as follows: at the 1236 site, 30.5% TT, 56.2% TC, and 13.3% CC; at 2677, 22.6% GG, 32.2% GT, 19.1% GA, 13.0% TA, 12.2% TT, and 0.9% AA; at 3435, 43.4% CC, 42.5% CT, and 14.2% TT. In Koreans, the frequencies of the alleles and genotypes of the MDR1 SNPs were similar to those of Asians but distinct from those of Caucasians. Of the 12 possible haplotypes, T-G-C, T-T-T, and C-G-C were observed most frequently, as they were in Chinese and Malays. However, the T-A-T and C-T-C haplotypes occurred more frequently in Koreans than in other Asians.

Conclusions: This study shows that the characteristics of the MDR1 SNPs of Koreans differ from those of other ethnic groups.

POSTER 7 10th ISS

ASSOCIATION OF GABRG2 POLYMORPHISMS WITH IDIOPATHIC GENERALIZED EPILEPSY

I-Ching CHOU[1], Chang-Hai TSAI[1,2], Lei WAN[3], Yu-An HSU[3], Tsai-Chung LEE[4], Fuu-Jen TSAI[1,3]

[1]Pediatrics, China Medical University Hospital, Taichung, Taiwan

[2]Asia University, Taichung, Taiwan

[3]Department of Medical Genetics, China Medical University Hospital, Taichung, Taiwan

[4]Graduate Institute of Chinese Medical Science, Chinese Medicine College, China Medical University, Taichung, Taiwan

Background: Missense mutations in the γ2 subunit of γ-aminobutyric acid (GABA) receptor gene have recently been described in families with idiopathic generalized epilepsies. We aimed to evaluate whether polymorphisms of the γ2 subunit of GABA receptor gene are associated with idiopathic generalized epilepsies.

Methods: A total of 77 children with idiopathic generalized epilepsies and 83 normal control subjects were included in the study. Polymerase chain reaction was used to identify the C/T and A/G polymorphisms of theγ2 subunit of GABA receptor gene on chromosome 5q33. Genotypes and allelic frequencies in both groups were compared.

Results: The γ2 subunit of GABA receptor (nucleotide position 3145 in intron G -> A) gene in both groups was not significantly different. In contrast, the γ2 subunit of GABA receptor (SNP211037)-C allele frequency in patients with idiopathic generalized epilepsies was significantly higher than that in healthy control subjects ($p = 0.002$). The odds ratio for developing idiopathic generalized epilepsies in individuals with theγ2 subunit of GABA receptor (SNP211037)-C/C genotype was 3.61 compared with individuals with theγ2 subunit of GABA receptor (SNP211037)-T/T genotype.

Conclusions: These data suggest that theγ2 subunit of GABA receptor gene might be one of the susceptibility factors for idiopathic generalized epilepsies. Further studies could be focused on the analysis of GABRG2 RNA and protein in children with idiopathic generalized epilepsies.

POSTER 8 10th ISS

MENTAL RETARDATION AND NEUROPSYCHIATRIC SYMPTOMS IN A FEMALE WITH COMPRESSION IN THE FIRST POLYALANINE TRACT OF THE ARX GENE

Yaman Z. EKSIOGLU, Amanda PONG, Masanori TAKEOKA

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

Background: The X-linked Aristaless-related homeobox gene, ARX, is a transcription factor implicated in GABAergic interneuron development and maintenance of circuitry in the forebrain, as well as development of pancreas and testes. ARX mutations are associated with mental retardation, lissencephaly, infantile spasms, Ohtahara syndrome and ambiguous genitalia in males. Despite syndromes with seizures, developmental delay and mood disorders; developmental delay and neuropsychiatric symptoms alone haven't been reported in females with ARX mutations.

Clinical Details: We describe a 12-year-old girl with cognitive delays in expressive and receptive language, reading, mathematics, social difficulties, anxiety, depression, and tantrums, despite normal achievement of early milestones without history of regression. ARX nucleotide sequence analysis, by City of Hope Clinical Molecular Diagnostic Laboratory (Duarte, CA), revealed that the proband was heterozygous for a novel mutation comprising a deletion of 6 base-pairs at nucleotides 330 in exon 2, resulting in polyalanine tract compression at amino acid 110 from 16 to 14 alanines.

Conclusions: This is the first reported case of cognitive delay with neuropsychiatric symptoms in a female associated with an ARX mutation that compresses the first polyalanine tract at amino acid 110. A similar mutation has been reported in a healthy male in an X-linked mental retardation family. However, presence of this novel mutation in this female with developmental delay and neuropsychiatric issues without appreciable CNS malformations warrants further assessment of this genetic phenomenon.

WEST SYNDROME IN A GIRL WITH COMPRESSION IN THE SECOND POLYALANINE TRACT OF THE ARX GENE

POSTER 9 10th ISS

Yaman Z. EKSIOGLU, Amanda PONG, Masanori TAKEOKA

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

Background: Aristaless-related homeobox gene, ARX located in Xp22.13, is a transcription factor crucial in forebrain, pancreas and testes development with particular role in GABAergic interneuron development and maintenance of circuitry. ARX mutations cause a pleiomorphic array of phenotypes including mental retardation, lissencephaly, infantile spasms, Ohtahara syndrome and ambiguous genitalia in males. However, heterozygous ARX mutations in females leading to infantile spasms and developmental delay have not been reported.

Clinical Details: We describe a 7-month-old girl with infantile spasms and developmental delay with regression (West syndrome) in the setting of a polyalanine tract compression in the second polyalanine tract in exon two of the ARX gene. ARX nucleotide sequence analysis (City of Hope Clinical Molecular Diagnostic Laboratory, Duarte, CA), revealed a heterozygous deletion of 24 base-pairs at nucleotides 441 to 464 in exon 2, resulting in polyalanine tract compression at amino acid 144 to 155 from 12 to 4 alanines (c.440-464 del 24 bp).

Conclusions: This is the first reported case of infantile spasms and progressive developmental delay in a girl in the setting of an ARX mutation that compresses the second polyalanine tract in exon two. Despite a report of this mutation, as a benign variant, in a healthy male member of an X-linked mental retardation family, presence of this mutation in a girl with West syndrome without appreciable CNS malformations warrants further genetic assessment of this entity.

INFLUENCES OF INTERLEUKIN-1β ON THE PROPENSITY OF HYPERTHERMIA--INDUCED SEIZURES IN DEVELOPING RATS

POSTER 10 10th ISS

Mitsumasa FUKUDA[1], Chiya SHINONAGA[1], Takehiko MORIMOTO[2], Yuka SUZUKI[3], Yasushi ISHIDA[1]

[1]Pediatrics, Ehime University Graduate School of Medicine, Toon, Ehime, Japan

[2]Ehime Disabled Children's Hospital, Matsuyama, Ehime, Japan

[3]Strong Epilepsy Center, University of Rochester Medical Center, Rochester, NY, USA

Background: Previous studies indicated that several cytokines influenced the seizure propensity in febrile seizures in childhood. In this study, we examined the role of Interleukin-1β (IL-1b) and Interleukin-1 receptor antagonist (IL-1ra) in hyperthermia-induced seizures in developing rats.

Methods: Twenty male Lewis rats (21-24 days old) were divided into two groups (IL-1β 500 ng and saline control groups). Two holes were made in the skull, one over the right frontal and one over the right occipital cortex, for EEG electrodes. And another hole was made over the left central cortex for the thermometer of the brain temperature. We applied human recombinant IL-1β intra-nasally 1h before seizures induced by moist heated air (45 degrees Celsius). The brain temperature at the appearance of seizure discharges on EEG, and the latency time from the hyperthermia onset until the appearance of seizure discharges on EEG were measured. And the same study using IL-1ra was performed.

Results: The brain temperature for the IL-1β group, 42.4±0.1 (mean±SE) degrees Celsius, was significantly lower than that for the control, 42.9±0.1 (P=0.030). The brain temperature for the IL-1ra group, 43.3±0.1 degrees Celsius, was significantly higher than that for the control, 42.9±0.1 (P=0.008), and the latency time for the IL-1ra group, 397±25 sec, was significantly longer than that for the control, 330±19 (P=0.046).

Conclusions: These results indicate that IL-1β plays a convulsive role in hyperthermia-induced seizures in developing rats.

POSTER 11 10th ISS

Withdrawn

POSTER 12 10th ISS

A COMPARISON WITH PROVOKED SEIZURES AND FEBRILE SEIZURES ASSOCIATED WITH MINOR INFECTIONS

Eun Ju LEE, Won Seop KIM

Pediatrics, Chungbuk National University School of Medicine, Cheongju, South Korea

Background: Provoked seizure is similar with febrile seizure but different. We studied seizures provoked by minor extracranial infections, to contrast them with febrile and provoked seizures.

Methods: We retrospectively studied 120 children with provoked and febrile seizures visited our hospital from January, 2000 to December, 2004. Among those, 36 patients were determined as provoked seizures and 84 patients as febrile seizures. We compared the distribution of minor infections between provoked seizures and febrile seizures, and studied the risk of subsequent unprovoked seizures after febrile and provoked seizures associated with minor infections.

Results: We analyzed the records of 120 children aged 1month to 15 years. The common etiologies as minor infections were gastroenteritis and respiratory infections. In febrile seizures, there was a significantly greater proportion of patients with respiratory infections (58%) and lesser proportion of those with gastroenteritis (25%). But there was a higher incidence of gastroenteritis (50%) in the provoked group. Comparing the distribution of etiologies between the patients with provoked seizures and those with febrile seizures seemed a significant difference (P=0.012). But, the risk for subsequent unprovoked seizure was no difference between the provoked seizures and febrile seizures (P=0.17).

Conclusions: The leading causes except brain involvement are gastroenteritis in patients with provoked seizure, and respiratory infection in those with febrile seizure. Thus follow-up about seizures associated with minor infections is needed.

POSTER 13 10th ISS

STATUS EPILEPTICUS INDUCED BY RESPIRATORY SYNCYTIAL VIRUS INFECTION IN PRETERM INFANTS

Mi-Sun YUM[1], Su Jeong YOU[2], Tae-Sung KO[1]

[1]Department of Pediatrics, University of Ulsan, College of Medicine, Ulsan, Korea

[2]Department of Pediatrics, Epilepsy Center, Inje University College of Medicine, Sang-gye Paik Hospital, Inje, Korea

Background: Respiratory syncytial virus (RSV) is an extremely common cause of childhood respiratory infection resulting in significant morbidity and mortality especially in young infants and premature babies. There have been a few reports about seizures or encephalopathy in children with RSV infection and no specific report about status epilepticus in RSV infection. We describe here refractory status epilepticus in two preterm babies with severe respiratory illness by RSV infection.

Clinical details: Two preterm babies, one with profound apnea and bradycardia without fever and the other with respiratory difficulty, in whom RSV antigens and cultures were positive in endotracheal aspirates, had been admitted. In the course of progressive respiratory illness, they showed persistent frequent subtle seizures and apneas with focal spike discharges on continuous EEG monitoring. The seizures were refractory to phenobarbital and diphenylhydantoin but ceased by continuous midazolam infusion. After several days with clinical improvement of respiratory illness, their seizures were stable on phenobarbital maintenance only. They could discharge without seizure on phenobarbital maintenance. At 3 months after discharge for one and 1 month for the other, no focal neurological deficit or seizure recurrence was detected.

Conclusion: Although rare, status epilepticus can be a form of neurologic manifestation of severe RSV infection in preterm baby. Pediatricians must be aware of their neurological manifestations. Continuous EEG monitoring is helpful for the diagnosis of the status epilepticus in infants.

ACTH THERAPY IN INFANTILE SPASMS AND CYTOMEGALOVIRUS INFECTION

POSTER 14 10th ISS

Dorota DUNIN-WASOWICZ, Sergiusz JOZWIAK, Jolanta KASPRZYK-OBARA
Department of Neurology and Epileptology, The Children's Memorial Health Institute, Warsaw, Poland

Background: It is known that corticosteroids increase brain levels of anticonvulsant neurosteroid. ACTH is usually recommended in infantile spasms, but suppresses every stage of immune response. That is the reason why in cases of infantile spasms and cytomegalovirus (HCMV) infection antiviral regimen may be considered.

Methods: Eleven infants, with infantile spasms and coexisting cytomegalovirus infection have been treated and followed up from the 1st January 1995 to the 31st December 2006. Specific antibodies, and DNA HCMV by qualitative PCR method in cerebrospinal fluid, blood, and urine were detected. All infants were treated with different antiepileptic drugs (AEDs) and ACTH before, during and after antiviral treatment with intravenous ganciclovir (GCV).

Results: One infant received ACTH before HCMV infection diagnosis, and demonstrated severe, life-dangerous cytomegalovirus infection with myocarditis and very high IgM antibodies titers, and had to be treated for 12 weeks with ganciclovir. Four infants with HCMV infection after one course of antiviral ganciclovir regimen received simultaneously ACTH and GCV. In neuroinfection cases, ACTH therapy was started even several months after finishing antiviral treatment. Cessation of spasms was achieved in five infants also with malformations of cortical development. In some of them with disappearance of hypsarrhythmia in EEG.

Conclusions: Cytomegalovirus may be epileptogenic and causes infantile spasms, but ACTH therapy should be avoided in an active HCMV infection. Antiviral regimen may be recommended before, or simultaneously with steroid therapy.

CLUSTER SEIZURES WITH DIARRHEA IN INFANCY: NOROVIRUS INFECTION IN AN ENDEMIC AREA

POSTER 15 10th ISS

Hsiu-Fen LEE, Ching-Shiang CHI, Chou-Huei CHEN, Po-Yen CHEN, Fang-Liang HUANG, Chieh-Chung LIN
Department of Pediatrics, Taichung Veterans General Hospital, Taichung, Taiwan

Background: Afebrile seizures in association with viral gastroenteritis had been reported, especially in Asia. The most common causative etiology was rotavirus. However, Norwalk-like virus, a small round structured virus (SRSV), had also been found the correlation with this disorder. We reported 3 cases presented cluster seizures with Norovirus gastroenteritis in this endemic period in Taiwan. It is the first report about the problem in this area.

Methods: From November 2006 to January 2007, we collected 3 cases with afebrile cluster seizures with diarrhea. The inclusion criteria was as follows: (1) normal development prior to the onset, (2) no underlying disorders nor neurological abnormalities, (3) frequency of afebrile seizures at least 2 episodes within 72 hours, (4) seizure onset between 2 months and 3 years of age, (5) family history of symptoms of acute gastroenteritis, (6) excluding febrile convulsion, central nervous system infections, well-known epileptic syndromes in infancy, electrolyte imbalance, head injury and intoxication. RNA from fecal samples was detected and genotyped by reverse transcription PCR (RT-PCR).

Results: Three cases, 2 male and 1 female, were aged 14 to 27 months. All of them had a normal neurological examination. The seizure patterns were generalized in 2 and partial in 1. The number of seizures per child ranged from 3 to 9. Most convulsions were short in terms of seconds to 5 minutes. No convulsions recurred after 3 days. The serum biochemistry was normal. Electroencephalogram (EEG) and computed tomography (CT) were performed and the results were normal. No pathogenic bacteria were grown in any of the stools. Enzyme immunoassay detection of rotavirus and adenovirus in the stools was negative, but the PCR of stool revealed Norovirus serotype 2. At the period of OPD follow-up, none had further convulsions and all had normal development milestones.

Conclusions: Recognition of cluster seizures with diarrhea in infancy should lead to reassurance to the parents. Investigations such as neuroimaging and EEG are usually normal and may not be necessary in most cases. Long-term anticonvulsant therapy is not usually warranted and the prognosis seems to be benign.

POSTER 16 10th ISS

A CLINICAL STUDY OF ACUTE SYMPTOMATIC SEIZURES IN CHILDREN

Keon-Su LEE[1], Won-Seop KIM[2]
[1]Pediatrics, Chungnam National University, Daejeon, Korea
[2]Pediatrics, Chungbuk National University, Cheongju, Korea

Background: To determine the incidence, etiology, sex, age, seizure type and prognosis of acute symptomatic seizures in children and evaluate the hypothesis that acute symptomatic status epilepticus (SE) is associated with an increased risk of subsequent unprovoked seizure compared with the risk of acute symptomatic seizure without SE.

Methods: Five hundred and sixty-eight convulsive children visited the Pediatric Department of Chungbuk National University Hospital from February 1991 to February 1999. Of these, 109 patients were determined as acute symptomatic seizure, and their medical record were reviewed.

Results: One hundred and nine children (59#boys, 50#girls) had acute symptomatic seizures, the ratio of male to female and the ages at the onset of first seizure were 1.18:1 and 1.58±2.53 years, respectively. Causes of acute symptomatic seizure in order of frequency were acute gastroenteritis (33.0%), encephalopathy (31.2%), metabolic/toxic disturbance (19.3%), CNS infection (11.0%), brain trauma (2.8%), cerebrovascular disease (1.8%) and CNS tumor (0.9%). At six months of follow-up, the incidence of a first unprovoked seizure was 28.4% for children with acute symptomatic seizure, 67.6% for those with encephalopathic cause, 44% for those with structural cause, and 0% for those with metabolic cause. At six months of follow-up, the risk of a first unprovoked seizure was significantly greater for those with acute symptomatic seizure with SE (100%) than without SE (22%).

Conclusion: The leading causes of acute symptomatic seizures were acute gastroenteritis. Age specific incidence was highest in the group aged 0-12 months. The incidence of subsequent unprovoked seizure was highest in the group of encephalopathy. The risk for subsequent unprovoked seizure was greater for those with SE than for those without SE and for those with abnormal EEG and abnormal findings of neuroimage.

POSTER 17 10th ISS

EARLY INFANTILE EPILEPSIES: SEIZURE TYPES AND EVOLUTIONS

Motomasa SUZUKI[1], Kazuya ITOMI[2], Kiyokuni MIURA[3], Hiroyuki KIDOKORO[4], Tetsuo KUBOTA[4], Toru KATO[1], Fumio HAYAKAWA[1], Akihisa OKUMURA[5], Koichi MARUYAMA[6], Yoko KONDO[7], Jun NATSUME[7], Kazuyoshi WATANABE[8]
[1]Pediatrics, Okazaki City Hospital, Okazaki, Japan, [2]Pediatric Neurology, Aichi Children's Health and Medical Center, Obu, Japan
[3]Pediatric Neurology, Aichi Prefectural Colony Central Hospital, Kasugai, Japan, [4]Pediatrics, Anjo-Kosei Hospital, Anjo, Japan
[5]Pediatrics, Juntendo University School of Medicine, Tokyo, Japan, [6]Pediatrics, Nagoya First Red Cross Hospital, Nagoya, Japan
[7]Pediatrics, Nagoya Graduate School of Medicine, Nagoya, Japan, [8]Aichi Syukutoku University, Aichi, Japan

Background: The aim of this study is to elucidate seizure types and evolutions of epilepsies of early infantile onset.

Methods: We retrospectively reviewed charts of patients with epilepsies beginning below 4 months of age, who were admitted to our institutions and followed for more than 1 year. We divided the patients into three groups of idiopathic, probably symptomatic and symptomatic epilepsies, and compared seizure types and their evolution among them.

Results: Sixty-three patients were studied. Sixteen of them were categorized as having idiopathic epilepsies, 21 probably symptomatic epilepsies, 26 symptomatic epilepsies. Twelve of the 16 patients with idiopathic epilepsies had the first seizure during the neonatal period, while the first seizure occurred after the neonatal period in 11 of 21 patients with probably symptomatic epilepsies and in 18 of 26 patients with symptomatic epilepsies. All patients with idiopathic epilepsies had partial seizures without changes of the seizure type. On the other hand, the initial seizure type was partial seizures or spasms in probably symptomatic and symptomatic epilepsies, and they often evolved to other seizure types such as partial seizures, spasms or brief tonic seizures.

Conclusions: Patients with idiopathic epilepsies consistently had partial seizures. In contrast, patients with probably symptomatic and symptomatic epilepsies often showed evolution of seizure types with development.

OVERALL PROGNOSIS OF ACTH THERAPY FOR WEST SYNDROME

POSTER 18 10th ISS

Yoko MATSUMOTO[1], Kazuhiro HAGINOYA[1], Mamiko ISHITOBI[1], Naomi HINO-FUKUYO[1], Noriko TOGASHI[1], Hiroyuki YOKOYAMA[1], Mitsutoshi MUNAKATA[1], Kazuie IINUMA[2]

[1]Department of Pediatrics, Tohoku University School of Medicine, Sendai, Japan

[2]Ishinomaki Red-Cross Hospital, Ishinomaki, Japan

Background: The primary purpose of this study is to examine the overall long-term effect of low dose synthetic adrenocorticotropic hormone (ACTH) therapy in addition to an initial effect of the therapy in children with West syndrome (WS). The secondary purpose of this study is to identify factors influencing the outcome of a synthetic ACTH.

Methods: Medical record of 117 patients diagnosed as having WS at Tohoku University between 1978 and 2004, were analyzed. Patients who achieved cessation of spasm before the ACTH therapy and second trial of the ACTH therapy were excluded. Remain 57 patients received 4 weeks regimen of synthetic ACTH. 31 patients received the synthetic ACTH 0.02mg/kg (0.8 IU/kg) and 26 patients received 0.015mg/kg (0.6 IU/kg) for 4 weeks. Initial and long term outcome were measured by complete cessation of seizures and disappearance of hypsarrhythmia on EEG.

Results: Immediately after the ACTH therapy, 44 (88%) patients showed cessation of seizure. Patients who had onset of spasms at age 4 months and older showed significant initial effect compared to patients whose onset was younger than 4 months (p=0.0038). 5.5 year overall long-term effect was 37%. Etiology and dosage of the ACTH had no significant effect on long-term outcome. There was no severe adverse effect related to ACTH therapy.

Conclusions: Low dose synthetic ACTH therapy benefited for seizure control as natural ACTH therapy for the initial outcome. This study indicated that 37% of patients had not experienced any seizure for at least 5.5 years after low dose synthetic ACTH therapy.

NEUROEPIDEMIOLOGY OF WEST SYNDROME AND EARLY INFANTILE EPILEPTIC ENCEPHALOPATHY IN MIYAGI PREFECTURE, JAPAN

POSTER 19 10th ISS

Naomi HINO-FUKUYO[1], Kazuhiro HAGINOYA[1], Kazuie IINUMA[2], Shigeru TSUCHIYA[1]

[1]Department of Pediatrics, Tohoku University School of Medicine, Sendai, Japan

[2]Department of Pediatrics, Ishinomaki Red-Cross Hospital, Ishinomaki, Japan

Background: West syndrome (WS) and early infantile epileptic encephalopathy (EIEE) are recognized as age-related catastrophic generalized epilepsy syndrome. There have been no studies on incidence rate of EIEE in the world, while that of WS have been reported from other prefecture of Japan and other countries.

Method: Based on the questionnaire to the pediatricians from thirty-two hospitals in Miyagi prefecture, medical records of WS and EIEE were retrospectively studied in the period from 2000 to 2005.

Result: Forty-five children (18 boys, 27 girls) developed WS, and one child was identified as EIEE during this period. The incidence rates of WS and EIEE were estimated as 4.2/10,000 and 0.1/10,000 live births, respectively.

Conclusion: The incidence rate of WS was similar to the previous report in Japan. We found that there is a great difference between incidence rates of WS and EIEE.

POSTER 20 10th ISS

EARLY ONSET IS A RISK FACTOR OF UNFAVORABLE PROGNOSIS OF MYOCLONIC-ASTATIC EPILEPSY

Takahito INOUE[1], Yukiko IHARA[1], Yuko TOMONO[1], Sawa YASUMOTO[1], Atsushi OGAWA[1], Masaharu OHFU[1], Akihisa MITSUDOME[2], Shinichi HIROSE[1]

[1]Department of Pediatrics, Fukuoka University, School of Medicine, Fukuoka, Japan

[2]International University of Health and Welfare, Fukuoka, Japan

Purpose: To investigate the relation between the onset age and the prognosis of myoclonic-astatic epilepsy (MAE).

Background: MAE is an idiopathic epileptic syndrome characterized by unique myoclonic seizures; myoclonic-astatic, or astatic seizures. Many patients are known to have an unfavorable prognosis while a recent study claimed that 68% of patients with MAE eventually achieved "seizure free". We hypothesized that the prognosis may have to do with age of the onset of MAE.

Methods: Medical history, EEG, and seizure symptoms were reviewed for nine children with MAE consisting of 5 boys and 4 girls, who had been followed for more than 2 years from the onset in our department.

Results: Ages of the onset of MAE in the patients ranged from 7 to 38 months with a mean of 24 months. Five patients were considered to have a favorable prognosis because the seizures had disappeared within 2 years from the onset while four had continued to have frequent attacks. The onset of MAE in the patient with refractory seizures was earlier than that in those with a favorable prognosis (7-24 months with a mean of 14 vs. 23-38 months with a mean of 32). All the patients with refractory seizures had moderate or severe mental retardation.

Conclusion: Early onset of MAE, which may give a considerable impact on developing central nervous system, was a sign of unfavorable prognosis including intellectual disability.

POSTER 21 10th ISS

DEVELOPMENTAL DELAY, EPILEPSY, AND NEONATAL DIABETES (DEND) SYNDROME: EARLY DIAGNOSIS AND ORAL SULFONYLUREA THERAPY POTENTIALLY IMPROVE NEURODEVELOPMENT

Akiko UEHARA[1], Ayako SOFUE[1], Tatsuya FUKASAWA[1], Makoto MORITA[1], Shinji HASEGAWA[1], Kazuyoshi WATANABE[1], Jun NATSUME[2]

[1]Department of Pediatrics, Nagoya Memorial Hospital, Nagoya, Japan

[2]Department of Pediatrics, Nagoya University Graduate School of Medicine, Nagoya, Japan

Background: Developmental delay, epilepsy, and neonatal diabetes (DEND) syndrome, first described in 2004, is characterized by heterozygous activating mutation in KCNJ11 gene encoding the Kir6.2 subunit of the ATP-dependent potassium channel. This channel distributes to pancreatic beta cells, muscles, and to brain, involving with insulin secretion, seizure susceptibility, and with neurodevelopment. Although these patients do not secrete insulin in response to glucose, they react to high-dose sulfonylurea. This therapy may control diabetes and potentially improves neurodevelopment in these patients.

Clinical detail: A four-month-old boy presented with developmental delay and spasms in cluster. Interictal EEG showed hypsarrhythmia compatible with West syndrome. Cranial MRI revealed no structural abnormalities. His blood glucose level was 280mg/dl, HbA1c was 9.8%, and subsequently he was diagnosed with antibody-negative diabetes mellitus. Genetic studies of the patient and his parents revealed de novo mutation (R50P) on the patient's KCNJ11 gene. Vitamin B6 and antiepileptic drugs were ineffective for spasms. ACTH-Z was started under close monitoring of blood glucose levels. Cessation of spasms and resolution of hypsarrhythmia were obtained. Following genetic diagnosis, his diabetic regimen was successfully switched from intensive insulin therapy to high-dose oral sulfonylurea (glibenclamide, 0.87mg/kg/day), resulting in acceptable levels of HbA1c to date.

Conclusion: We describe the first Japanese case of DEND syndrome diagnosed at early age. ACTH-Z can be given safely, and early intervention with sulfonylurea not only controls diabetes, but potentially improves neurodevelopment.

CLINICAL AND ELECTROPHYSIOLOGICAL CHARACTERISTICS OF INFANTILE SPASMS OBSERVED IN CHILDREN IN THE REPUBLIC OF KAZAKHSTAN (INFANTILE SPASMS, DYSGENESIS OF BRAIN, INTRAUTERINE INFECTION, PERINATAL ENCEPHALOPATHY, TUBEROUS SCLEROSIS)

POSTER 22 10th ISS

M. LEPESSOVA, B. MYRZALIYEVA, Z. MEDETBEKOWA, G. TAIROVA

Department of Child Neurology, Almaty State Post-graduate Institute, Almaty, Kazakhstan

Background: From 2003 to 2006 we evaluated 53 children with infantile spasms seen at department of child neurology of city hospital.

Methods: The clinical, EEG and neuroradiological examinations.

Results: The symptomatic nature of the attacks was revealed in 91% of the patients. The etiology of the infantile spasms: dysgenesis of brain – 37.5%, tuberous sclerosis complex – 12.5 %, intrauterine infection -16,6%, perinatal encephalopathy – 18.8%, traumas – 4.1%. The debut of the spasms in the age of 3-6 months (69%), flexor spasms – 35.5%, extensor spasms – 21.5%, mixed forms - 43%. Dissymmetric spasms were observed in 37% cases. EGG examination revealed typical hypsarhythmia in 56.6% of all the patients, atypical hypsarhythmia- in 62% with symptomatic spasms and in 9.4% of children no pathological changes were revealed in EEG. The neuroradiological examination (CT/ MRT): dysgenesis of the brain was revealed in 33.9% of all patients(18), in 16.9%(9) the dysgenesis combined with periventricular leukomalacia, selective neuronal necrosis; in 15%(8)- subependymal cysts, vascular plexus cysts, focuses of reduced density; intracerebral calcifications were revealed in 6 children (11.3%).

Conclusions: In genesis of the infantile spasms a growing importance of the intrauterine herpesvirus infection draws attention. With symptomatic infantile spasms most of the attacks have an asymmetrical character with focal component that witnesses to a high risk of the structural defect of the brain and an electroencephalogram defines atypical hypsarythmia. Neuroradiological results confirm etiological characteristic of the symptomatic spasms.

EPILEPSY PRESENTING AS MAJOR MANIFESTATION OF PRIMARY BRAIN TUMOR IN CHILDREN

POSTER 23 10th ISS

Ching-Wan TSAI, Kun-Long HUNG

Department of Pediatrics, Cathay General Hospital, Taipei, Taiwan

Background and Objectives: The purpose of this study is to review the detailed seizure history of a population of children with brain tumor to identify the etiology especially those presented only with seizure or epilepsy initially.

Methods: A retrospective chart review of children with brain tumor in the past 10years was conducted to find out those presented with epilepsy. We analyzed the medical data included age of seizure onset, age of tumor diagnosis, seizure type, neurologic examination, image finding, EEG finding and tumor pathology.

Results and Conclusion: During 1995 to 2005, there were 7 children presented with epilepsy as initial symptom among 45 patients suffering from childhood brain tumor in our hospital. The seizure was mainly partial in nature. Two children presented with additional developmental delay. Physical examination revealed no specific neurological signs. The EEG findings were focal discharges, with focal or generalized slow background activities in cases. The duration from seizure onset to tumor diagnosis varied from 1 week to several years. The tumor etiologies included glioma in 3 patients, ependymoma in 1, giant cell astrocytoma in 1 and fibrolipoma originated from scalp in 1. One case of low grade glioma diagnosed initially turned to be malignant change 6 months later. The diagnosis of brain tumor is somewhat difficult for those presenting with epilepsy only. Detailed history taking, through physical examination, complete check up and appropriate neuroimage studies are the important clues for the final diagnosis.

POSTER 24 10th ISS

DIFFUSION WEIGHTED IMAGE ABNORMALITIES AND GLUCOSE HYPO-METABOLISM IN PATIENTS WITH PROLONGED FEBRILE SEIZURES

Jun NATSUME[1,3], Neda BERNASCONI[2], Megumi MIYAUCHI[1], Misako NAIKI[1], Taro YOKOTSUKA[1], Koichi MARUYAMA[3], Ayako SOFUE[1], Andrea BERNASCONI[2]

[1]Department of Pediatrics, Nagoya University, Nagoya, Japan

[2]Department of Neurology and Neurosurgery, Montreal Neurological Institute and Hospital, McGill University, Montreal, Canada

[3]Department of Pediatrics, Japanese Red Cross Nagoya First Hospital, Nagoya, Japan

Background: There is continued debate on whether status epilepticus can cause hippocampal damage leading to temporal lobe epilepsy. We assessed functional abnormalities in the limbic circuitry using FDG-PET in children who had diffusion weighted image (DWI) abnormalities in hippocampus after prolonged febrile seizures (PFS).

Methods: DWI showed unilateral hippocampal hyperintensity in three of 12 patients with PFS in our previous study. We performed FDG-PET in these three patients two years after PFS. Region of Interests (ROIs) generated from each patient's MRI were placed on temporal lobes and other anatomical areas. Radioactivity in each ROI was measured and asymmetry index (AI) for the value of each homologous pair was calculated: AI(X) = (CX-IX)/[(CX+IX)/2] x 100 %, where IX is the value on the side ipsilateral to the DWI abnormality, and CX is the value of its homologue on the contralateral side.

Results: Hypometabolism was observed in the temporal lobes ipsilateral to the DWI abnormality in two patients by visual inspection. ROI analysis revealed reduced activity in the ipsilateral hyppocampi of all patients and AIs were 11-22 %. In other homologous pairs, AIs larger than 10 % were seen in the lateral temporal lobe and amygdala of one patient, and in the thalamus of other one patient.

Conclusions: In children who had DWI abnormalities in hippocampus after PFS, functional abnormality in limbic system is already seen in the early stage after PFS.

POSTER 25 10th ISS

FDG-PET STUDY OF PATIENTS WITH GENETICALLY CONFIRMED PATIENTS WITH SEVERE MYOCLONIC EPILEPSY IN INFANCY

Kazuhiro HAGINOYA[1], Noriko TOGASHI[1], Taro KITAMURA[1], Mitsugu UEMATSU[1], Tomoko KOBAYASHI[1], Yoko MASTSUMOTO[1], Yosuke KAKISAKA[1], Keisuke WAKUSAWA[1], Naomi HINO-FUKUYO[1], Mamiko ISHITOBI[1], Kazuie IINUMA[2], Shigeru TSUCHIYA[1], Tomohiro KANETA[3], Kazuhiro YAMAKAWA[4]

[1]Department of Pediatrics, Tohoku University School of Medicine, Sendai, Japan

[2]Department of Pediatrics, Ishinomaki Red-Cross Hospital, Ishinomaki, Japan

[3]Department of Radiology, Tohoku University School of Medicine, Sendai, Japan

[4]Laboratory for Neurogenetics, RIKEN Brain Science Institute, Saitama, Japan

Background: The FED-PET analysis of genetically confirmed patients with SMEI has not been reported so far. Understanding the process of brain dysfunction along with aging in SMEI may provide more effective strategy for the treatment of patients with SMEI.

Methods: FDG-PET was performed on 7 patients with SMEI. The mutation analysis of SCN1A revealed missense mutation in 2, and flameshift mutation in 4 patients. The patients' age on the PET study was 2, 2, 2, 3, 6, 13, and 29 years-old, respectively. The results was inspected visually and evaluated semi-quantitatively. Those were compared with 7 control patients. The patients' DQ/IQs were 62, 52, 64, 35, 30, 22, <25, respectively.

Results: Normal glucose metabolism pattern was obtained from four younger cases aged bellow 3 years old. On the other hand, significant abnormality was observed in 3 older patients whose interictal EEG showed frequent irregular multifocal spike-waves over bilateral frontal to parietal areas. Hypometabolism of bilateral temporo-parietal association cortex was detected in two older cases. Diffuse hypometabolism of bilateral fronto-parieto-temporal areas was observed in a case aged 6. These abnormalities are not clearly detected by ECD-SPECT study.

Conclusion: FDG-PET in patients with SMEI revealed for the first time progressive deterioration of cerebral glucose metabolism along with aging. It is not known at present whether these progressive dysfunctions of cerebral cortex are secondary to the repetitive seizure activity or a feature of SMEI itself.

ACTIVATION OF SUBCORTICAL GRAY MATTER DURING SPASMS IN PATIENTS WITH WEST SYNDROME: SUBTRACTION SPECT

POSTER 26 10th ISS

Yosuke KAKISAKA[1], Kazuhiro HAGINOYA[1], Mamiko ISHITOBI[1], Noriko TOGASHI[1], Taro KITAMURA[1], Keisuke WAKUSAWA[1], Ikuko SATO[1], Naomi HINO-FUKUYO[1], Mitsutoshi MUNAKATA[1], Hiroyuki YOKOYAMA[1], Kazuie IINUMA[1], Tomohiro KANETA[2], Shigeru TSUCHIYA[1]

Departments of [1]Pediatrics and [2]Radiology, Tohoku University School of Medicine, Sendai, Japan

Background: West syndrome, in which major of its pathophysiology remains to be unknown, is an age-dependent epileptic encephalopathy with multiple etiology and with diverse psychomotor outcome. Though evaluation of cerebral blood change during spasms using SPECT has been reported, conventional side-by-side analysis of ictal and interictal images have prevented us form achieving clear, objective results. In this study, we evaluate ictal blood flow changes by subtraction ictal SPECT analysis, subtracting interictal images from ictal ones.

Methods: Twelve patients, including 9 symptomatic cases, with West syndrome are included in this study. When spasms are observed to repeat over 2 times, we regard it as ictal phase and soon have injected tracer, 99mTc-ethyl cysteinate dimmer (ECD).

Results: All but two cases had multifocal cortical hyperperfusion probably due to secondary propagation of epileptic discharges. Five out of 12 patients showed hyperperfusion of subcortical gray matter especially basal ganglia and thalamus. Two cases showed both focal cortical hyperperfusion corresponding to MRI lesion and/or EEG abnormality and subcortical grey matter hyperperfusion.

Conclusion: We believe this presentation is important because subcortical activation is disclosed semi-quantitatively, suggestive that genesis of spasms is related to subcortical gray matter. Two cases showing both focal cortical and subcortical gray matter hyperperfusion imply that focal epileptic activities trigger generation of spasms via subcortical structure.

CHARACTERISTICS OF SPECT AND PET OF BRAIN IN SEVERE MYOCLONIC EPILEPSY: A CASE REPORT

POSTER 27 10th ISS

Shyi-jou CHEN[1], Kai-ping CHANG[2], Chin-chin WANG[1]

[1]Pediatrics, Tri-Service General Hospital, Taipei, Taiwan,

[2]Pediatrics, Taipei-Veterans General Hospital, Taipei, Taiwan.

Background: The clinical characteristics of Severe Myoclonic Epilepsy in infancy (SMEI) are repeated febrile hemiclonic or generalized status epilepticus since first year of life, typically around 6 months and followed by the evolution of afebrile seizures including myoclonic, absence, atonic and partial seizures between 1 and 4 years. Developmental progress is initially normal but slows in the second year. Hippocampal sclerosis in SMEI had been documented from MRI. However, the progressive MRI resulted and the correlation among clinical, MRI, SPECT and PET had not been entirely reported.

Clinical details: A 4-year-old male suffered from prolonged febrile seizure at his age of 9 month. Subsequently, he started frequent generalized or unilateral prolonged febrile and afebrile seizure 1-2 fits in a week. Additionally, myoclonic epilepsy occurred. Thereafter, his seizures were progressive to refractory, and he developed learning disability and cognitive deterioration. At the age of 4 year-old, his brain MRI showed decreased NAA/Cr ratio of bil. Hippocampus on MRS. Brain SPECT demonstrated homogenous perfusion in the cerebral cortex with relatively decreased uptake in lt. fronto-parietal region, and in bil. thalamus. Moreover, we examined 18F-FDG PET/CT of brain scan showed lower rCMR in major area which including left temporal, right limbic lobe and right thalamus respectively.

Conclusion: The highly parallel areas of hypoperfusion obtained from SPECT and PET may correlate with the clinical manifestation of neuro-psychiatric deterioration in this case with SMEI.

CURRICULUM VITAE
AND
SELECTED PUBLICATION LISTS
OF INVITED SPEAKERS

Shinichi HIROSE

Present Position

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

Appointments

1980 Resident, Fukuoka University Hospital
1982 Clinical Fellow in Pediatrics, Fukuoka University Hospital
1984 Graduate research in Biochemistry, Fukuoka University School of Medicine
1988 Research associate, Institute of Pathology, Case Western Reserve University, Cleveland Ohio
1992 Instructor in Pediatrics, Fukuoka University Hospital
1994 Assistant Professor, Department of Pediatrics, School of Medicine Fukuoka University
1997 Associate Professor, Department of Pediatrics, School of Medicine, Fukuoka University
2006- Present position

Selected Publications

1. Hirose S. A new paradigm of channelopathy in epilepsy syndromes: Intracellular trafficking abnormality of channel molecules. *Epilepsy Res* 2006;70(Suppl.1):S206-17
2. Hirose S, Mitsudome A, Okada M, Kaneko S. Genetics of idiopathic Epilepsies. *Epilepsia* 2005;46:38-43
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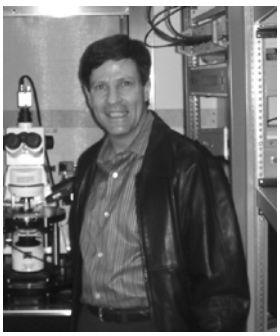
5. Hirose S, Okada M, Yamakawa K, Sugawara T, Fukuma G, Ito M, Kaneko S, Mitsudome A. Genetics abnormalities underlying familial epilepsy syndromes. *Brain Dev* 2002;24:211-22

Alan L. GOLDIN



Present Positions

Professor, Department of Anatomy & Neurobiology, U. California, Irvine, USA

Appointments

1983 Research Fellow, Department of Chemistry, California Institute of Technology
1986 Senior Research Fellow, Department of Biology, California Institute of Technology
1988 Assistant Professor, Department of Microbiology and Molecular Genetics, U. California, Irvine
1994 Associate Professor, Department of Microbiology and Molecular Genetics, U. California, Irvine
1998 Professor, Department of Microbiology and Molecular Genetics, U. California, Irvine
2004- Present position

Selected Publications

1. Goldin AL, Barchi RL, Caldwell JH, Hofmann F, Howe JR, Hunter JC, Kallen RG, Mandel G, Meisler MH, Berwald-Netter Y, Noda M, Tamkun MM, Waxman SG, Wood JN, Catterall WA. Nomenclature of voltage-gated sodium channels. *Neuron* 2000;28:365-8
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Alexis ARZIMANOGLOU

Present Positions

Consultant Neurologist and Child Neurologist and Head of the Epilepsy Program
Child Neurology and Metabolic Diseases Dpt. University Hospital ROBERT DEBRE, Paris, and
Institute for Children and Adolescents with Epilepsy - IDEE, Lyon, France

Appointments

1987 Assistant Neurologist, Department of Neurology, University Hospital PITIE-SALPETRIERE
1991 Consultant Neurologist / Child Neurologist / Epileptologist, Department of Neurology, Department of Paediatrics in charge of the Child Neurology and of the children's EEG Units, University Hospital PITIE - SALPETRIERE, Paris, France
1998- Present position

Editorial Activities

Editor-in-Chief of the journal *Epileptic Disord*, Associate Editor of the *Eur J Paediatr Neurol*.

Selected Publications

1. Laurent A, Arzimanoglou A. Cognitive impairments in children with nonidiopathic temporal lobe epilepsy. *Epilepsia* 2006;47:S2:99-102
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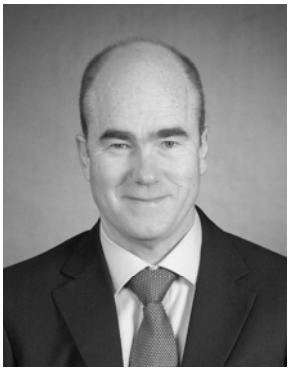
Books: Thomas P, Arzimanoglou A. Epilepsies. Masson Ed. 2001. Arzimanoglou A, Guerrini R, Aicardi J. Aicardi's epilepsy in children. 3rd edi. Lippincott & Williams 2004. Arzimanoglou A, Aldenkamp A, Cross H, Lassonde M, Moshe SL, Schmitz B (editors). Cognitive dysfunction in children with temporal lobe epilepsy. JLE 2005

Kevin J. STALEY



Present Position

Professor of Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Appointments

1988 Instructor in Pediatrics, University of California San Diego
1989 Instructor in Neurology, Stanford University
1991 Assistant Professor in Neurology, University of Colorado
1997 Associate Professor in Neurology, University of Colorado
2004 Professor, Pediatrics University of Colorado
2006 Staff Neurologist, Massachusetts General Hospital
2006 Chief, Section of Pediatric Neurology, Departments of Neurology and Pediatrics, Massachusetts General Hospital

Selected Publications

1. Staley KJ, Longacher M, Bains J, Yee A. Presynaptic modulation of CA3 network activity. *Nat Neurosci* 1998; 1:201-9
2. Bains JS, Longacher JM, Staley KJ. Reciprocal interactions between CA3 network activity and strength of recurrent collateral synapses. *Nat Neurosci* 1999;2:720-6
3. Dzhala V, Staley KJ. Endogenous GABA initiates seizure activity in the neonatal hippocampal slice preparation. *J Neurosci* 2003;23:1840-6
4. Dulla C, Dobelis P, Pearson T, Frenguelli BG, Staley KJ (communicating author), Masino SA. Adenosine and ATP link PCO2 to cortical excitability via pH. *Neuron* 2005;48:1011-23
5. Dzhala VI, Talos DM, Sdrulla DA, Brumback AC, Mathews GC, Benke TA, Delpire EJ, Jensen FE, Staley KJ. NKCC1 transporter facilitates seizures in the developing brain. *Nat Medicine* 2005;11:1205-13.

John W. SWANN

Present Positions

Professor, Departments of Pediatrics and Neuroscience, Baylor College of Medicine, Houston, Texas, USA

Appointments

1992- Scientific Director, The Gordon and Mary Cain Pediatric Neurology, Research Foundation Laboratories Texas Children's Hospital
1992- Present positions
2002- Director, Interdepartmental Training Program "Brain Disorders and Development", Baylor College of Medicine
2005- Professor, Graduate Program in Translational Biology and Molecular Medicine Baylor College of Medicine

Selected Publications

1. Lee CL, Hannay J, Hrachovy R, Rashid S, Antalffy B, Swann JW. Recurrent seizures in infant rats produce spatial learning deficits without a substantial loss of hippocampal pyramidal cells. *Neurosci* 2001;107:71-84
2. Swann JW. Recent experimental studies of the effects of seizures on brain development. *Prog Brain Res* 2002, 135:391-3
3. Swann JW. The impact of seizures on developing hippocampal networks. *Prog Brain Res* 2004;147: 347-54
4. Stafstrom CE, Moshé SL, Swann JW, Nehlig A, Jacobs MP, Schwartzkroin PA. Models of pediatric epilepsies: strategies and opportunities. *Epilepsia* 2006;47:1407-14
5. Swann JW, Le JT, Lee CL. Recurrent seizures and the molecular maturation of hippocampal and neocortical glutamatergic synapses. *Dev Neurosci* 2007;29: 168-78

Solomon L. MOSHÉ

Present Position

Professor of Neurology, Neuroscience and Pediatrics Albert Einstein College of Medicine (AECOM), Bronx, New York, USA.

Appointments

1984 Associate Professor of Neurology, Albert Einstein College of Medicine (AECOM)
1985 Associate Professor of Pediatrics, AECOM
1986- Director Clinical Neurophysiology, AECOM / Montefiore Medical Center
1991- Professor of Pediatrics, AECOM
1995- Director, Child Neurology, AECOM / Montefiore Medical Center
1989- Present position
1997- Tenured Professor of Neurology, Neuroscience and Pediatrics, AECOM
2000- Vice Chairman, Department of Neurology, AECOM

Selected Publications

1. Holmes GL, Moshé SL, Jones RH, Jr (Eds). Clinical Neurophysiology of Infancy and Childhood. Elsevier (2005).
2. Veliskova J, Moshé SL. Update on the role of substantia nigra pars reticulata in the regulation of seizures. *Epi Curr* 2006;6: 83-7
3. Kyrozis A, Chudomel O, Moshé SL, Galanopoulou AS. Sex-dependent maturation of GABAA receptor- mediated synaptic events in rat substantia nigra reticulate. *Neurosci Lett* 2006;398:1-5
4. Velisek L, Veliskova J, Giorgi, FS, Moshé SL. Sex-specific control of flurothyl –induced tonic-clonic seizures by the substantia nigra pars reticulate during development. *Exp Neurol* 2006;201:203-11
5. Giorgi FS, Velíšková J, Chudomel O, Kyrozis O, Moshé SL. The role of substantia nigra pars reticulata in modulating clonic seizures is determined by testosterone levels during the immediate postnatal period. *Neurobiol Dis* 2006;25:73-9

Asuri PRASAD

Present Position

Associate Professor, Department of Pediatrics and Clinical Neurosciences, Faculty of Medicine, University of Western Ontario, London, Ontario, Canada

Appointments

1980 MBBS (Bachelor of Medicine Bachelor of Surgery), University of Delhi, India
1984 MD (Pediatrics), Post Graduate Institute of Medical Education and Research, Chandigarh, India
1987 MRCP (UK), The Royal College of Physicians London, UK
1992 FRCPC, The Royal College of Physicians and Surgeons of Canada (Pediatrics) Certified in Pediatrics
1996 FRCPC (Neurology) Certification in Neurology and Child Neurology
1992 Diplomate in Pediatrics, American Board of Pediatrics, Re-certified 2000
1996 Diplomate in Neurology and Child Neurology, American Board of Psychiatry &Neurology. Fellow, American Academy of Neurology (FAAN)
2004 FRCPE, Elected Fellow of the Royal College of Physicians of Edinburgh (UK)

Selected Publications

1. Prasad AN. Argininemia: a treatable genetic cause of progressive spastic diplegia simulating cerebral palsy – case reports and review of literature. *J Child Neurol* 1997;12:301-9
2. Prasad AN. Recent Advances in the Genetics of Epilepsy: Insights from Human and Animal studies. *Epilepsia* 1999;40 1329-52
3. Prasad C, Prasad AN, Chodirker BN, Lee C, Dawson AK, Jocelyn LJ, Chudley AE. Genetic evaluation of pervasive developmental disorders; the terminal 22q13 deletion syndrome may represent a recognizable phenotype. *Clin Genetics* 2000;57;103-9 (50% contribution)
4. Funk CB, Prasad AN. Neuropathological, biochemical and molecular findings in a glutaric acidemia type 1 cohort. *Brain* 2005;128:711-22
5. Birdi K, Prasad AN, Prasad C, Chodirker B, Chudley AE. The floppy infant: retrospective analysis of clinical experience (1990-2000) in a tertiary care facility. *J Child Neurol* 2005;20:803-8

Tallie Z. BARAM

Present Position

Professor in the Departments of Pediatrics, Anatomy / Neurobiology and Neurology at the University of California, Irvine (UCI), USA

Appointments

1995- Present position
1995- Danette Shepard endowed chair in Neurological Sciences
2000- Scientific Director of the UCI Epilepsy program
2002- Founder and Executive Committee chair, UCI Epilepsy Research Center

Selected Publications

1. Brunson KL, Kramar E, Lin B, Chen Y, Colgin LL, Yanagihara TK, Lynch G, Baram TZ. Mechanisms of late-onset cognitive decline after early-life stress. *J Neurosci* 2005;259328-38
2. Avishai-Eliner S, Brunson KL, Sandman CA, Baram TZ. Stressed out, or *in utero*? *Trends Neurosci* 2002;25:518-24
3. Brunson KL, Khan N, Eghbal-Ahmadi, Baram TZ. ACTH acts directly on amygdala neurons to down-regulate corticotropin releasing hormone gene expression. *Ann Neurol* 2001;49:304-13
4. Brunson KL, Eghbal-Ahmadi M, Chen Y, Baram TZ. Progressive hippocampal cell loss and long-term cognitive dysfunction induced by early-life administration of corticotropin releasing hormone reproduce the effects of early-life stress. *Proc Nat Acad Sci* 2001;98:8856-61
5. Baram TZ, Hatalski CG. Neuropeptide-mediated excitability: A key triggering mechanism for seizure generation in the developing brain. *Trends Neurosci* 1998;21:471-6

Ulrich SCHRIDDE

Present Position

Department of Neurology, Yale University School of Medicine, New Haven, CT, USA

Appointments

1999 Research Assistant, NICI, Dept. of Biological Psychology, Radboud University Nijmegen
2000 Ph.D. Student, NICI, Dept. of Biological Psychology, Radboud University Nijmegen
2004- Post-doctoral Associate, Dept. of Neurology, Yale University School of Medicine

Selected Publications

1. Schridde U, van Luijtelaar G. The role of hippocampal theta activity in sensory gating in the rat. *Physiol Behav* 2001;74:257-66
2. Schridde U, van Luijtelaar G. The influence of strain and housing on two types of spike-wave discharges in rats. *Genes Brain Behav* 2004;3:1-7
3. Schridde U, van Luijtelaar, G. Corticosterone increases spike-wave discharges in a dose and time dependent manner in WAG/Rij rats. *Pharmacol Biochem Behav* 2004;78:369-75
4. Schridde U, van Luijtelaar G. The role of the environment on the development of spike-wave discharges in two strains of rats. *Physiol Behav* 2005;84:379-86.
5. Schridde U, Strauss U, Bräuer AU, Luijtelaar G. Environmental manipulations early in development alter seizure activity, Ih and HCN1 protein expression later in life. *Eur J Neurosci* 2006; 23:3346-58

Ganeshwaran H. MOCHIDA

Present Position

Instructor in Neurology, Harvard Medical School, Boston, Massachusetts, USA

Appointments

1994 Resident in Pediatrics, Keio University Hospital, Tokyo, Japan
1995 Resident in Pediatrics, Massachusetts General Hospital
1996 Resident in Pediatric Neurology, Massachusetts General Hospital
1999 Fellow in Neurology (Neurogenetics / Neurodevelopment), Harvard Medical School
Fellow, Clinical Investigator Training Program, Harvard/MIT Division of Health Sciences and Technology
Research Fellow in Neurology, Beth Israel Deaconess Medical Center, Boston, MA
2001 Assistant in Neurology, Massachusetts General Hospital
2001- Present position

Selected Publications

1. Bond J, Roberts E, Mochida GH, Hampshire DJ, Scott S, Askham JM, Springell K, Mahadevan M, Crow YJ, Markham AF, Walsh CA, Woods CG. ASPM is a major determinant of cerebral cortical size. *Nat Genet* 2002;32:316-20
2. Rajab A*, Mochida GH*, Hill A, Ganesh V, Bodell A, Riaz A, Grant PE, Shugart YY, Walsh CA. A novel form of pontocerebellar hypoplasia maps to chromosome 7q11-21. *Neurology* 2003;60:1664-7 *These authors contributed equally to this work.
3. Kouprina N*, Pavlicek A*, Mochida GH*, Solomon G, Gersch W, Yoon YH, Collura R, Ruvolo M, Barrett JC, Woods CG, Walsh CA, Jurka J, Larionov V. Accelerated evolution of the *ASPM* gene controlling brain size begins prior to human brain expansion. *PLoS Biol* 2004;2:e126 *These authors contributed equally to this work.
4. Mochida GH, Rajab A, Eyaid W, Lu A, Al-Nouri D, Kosaki K, Noruzinia M, Sarda P, Ishihara J, Bodell A, Apse K, Walsh CA. Broader geographic spectrum of Cohen syndrome due to *COH1* mutations. *J Med Genet* 2004;41:e87
5. Shen J, Eyaid W, Mochida GH, Al-Moayyad F, Bodell A, Woods CG, Walsh CA**.** ASPM mutations identified in patients with primary microcephaly and seizures. *J Med Genet* 2005;42:725-9

Harvey B. SARNAT

Present Positions

Professor of Pediatrics, Pathology (Neuropathology) and Clinical Neuroscience, University of Calgary Faculty of Medicine, Calgary, Alberta, Canada

Appointments

1973 Assistant Professor of Neurology and Pediatrics, St. Louis University School of Medicine
1976 Lecturer and Consultant Neurologist, University of Western Australia, Perth, W.A., Australia
1977 Associate Professor of Neurology and Pediatrics, St. Louis University School of Medicine
1978 Associate Professor of Pediatrics, Neurology and Pathology, University of Arkansas for Medical Sciences
1981 Associate Professor of Paediatrics, Pathology and Clinical Neurosciences, University of Calgary Faculty of Medicine
1984 Professor of Paediatrics, Pathology and Clinical Neurosciences, University of Calgary Faculty of Medicine
1992 Professor of Pediatrics (Neurology) and Pathology (Neuropathology), University of Washington School of Medicine, Washington
1992 Herman and Faye Sarkowsky Professor of Pediatric Neurology (Endowed Chair) and Head, Division of Pediatric Neurology
2001 Professor of Pediatrics (Neurology) and Pathology (Neuropathology), University of California at Los Angeles (UCLA), School of Medicine, California
2004- Present position

Selected Publications

1. Sarnat HB, Born DE. Synaptophysin immunocytochemistry with thermal iontensification: a marker of terminal axonal maturation in the human fetal nervous system. *Brain Dev* (Tokyo) 1999;21:41-50
2. Synaptogenesis in the human fetal and neonatal brain. Synaptophysin as an immunocytochemical marker of synapse formation. 2007;submitted
3. Guangnan L, Pleasure SJ. Morphogenesis of the dentate gyrus: What are we learning from mouse mutants? *Dev Neurosci* 2005;27:93-9
4. Bennett MK, Scheller RH. A molecular description of synaptic vesicle membrane trafficking. *Annu Rev Biochem* 1994;63:63-100
5. Swann JW, Le JW, Lee JT, Chong L. Recurrent seizures and the molecular maturation of hippocampal and neocortical glutamatergic synapses. *Dev Neurosci* 2007;29:168-78

Paolo CURATOLO

Present Position

Professor of Pediatric Neurology and Psychiatry, Department of Neuroscience, University of Rome, Italy

Appointments

1974 Graduation at Catholic University Medical School, Rome
1974 Postgraduate Education on Child Neurology and Psychiatry, University La Sapienza, Rome
1979 Assistant Professor of Pediatric Neurology, University La Sapienza, Rome
1980 Associate Professor of Pediatric Neurology University La Sapienza, Rome
1990 Professor of Pediatric Neurology, University D'Annunzio, Chieti
1994 Professor of Pediatric Neurology and Psychiatry, University of Rome Tor Vergata

Selected Publications

1. Curatolo P, Bombardieri R, Cerminara C. Current management for epilepsy in tuberous sclerosis complex. *Curr Opin Neurol* 2006;19:119-23
2. Curatolo P, Bombardieri R, Verdecchia M, Seri S. Intractable seizures in tuberous sclerosis complex: from molecular pathogenesis to the rationale for treatment. *J Child Neurol* 2005;20:318-25
3. Romanelli P, Verdecchia M, Rodas R, Seri S, Curatolo P. Epilepsy surgery for tuberous sclerosis. *Pediatr Neurol* 2004;31:239-47
4. Curatolo P, Verdecchia M, Bombardieri R. Tuberous sclerosis complex: a review of neurological aspects. *Eur J Paediatr Neurol* 2002;6:15-23
5. Curatolo P, Verdecchia M, Bombardieri R. Vigabatrin for tuberous sclerosis complex. *Brain Dev* 2001;23:649-53

Performer of *Echigo Jishi* in 'WELCOME CULTURAL PERFORMANCE' on DAY1

Junomaru HANAYAGI

Mistress of *Nihon Buyo*, HANAYAGI in the style

What is *Nihon Buyo* (Japanese Classical Dance)?

The original form of "*nihon buyo*" is recorded in Japan's oldest historybook "*Kojiki*" that was completed in 712 AD. It describes how a goddess "*Amenouzume-no-mikoto*" devoted herself to dancing; she put grass on her dress and hair for decorations, clasped a bundle of bamboo leaves in her hand, and stamped her feet on a large pail. Today approximately 5,000 professional dancers are actively working in *nihon buyo* circles, and giving their performances at nationwide venues.

ECHIGO JISHI (The Lion of *Echigo*), performed in 'WELCOME CULTURAL PERFORMANCE' on DAY1

This dance portrays a story from the *Edo* Era in which a lion dance performer from *Echigo* (Niigata area in Japan) arrives in *Edo* (Tokyo) and makes a living walking through the town, dancing and performing other forms of entertainment.

International Symposia in Past 6 years Organized by Infantile Seizure Society

Year	Theme	Invited Faculties (Japanese excluded)	Publications
2001	West Syndrome and Other Epileptic Encephalopathies	Appleton RE, Aysun S, Baram TZ, Chiemchanya S, Chugani H, Curatolo P, Dulac O, Fusco L, Hancock E, Hwang YS, Kalra V, Koul R, Liu ZS, Ong HT, Osborne JP, Qin J, Riikonen R, Salonga AM, Scheffer IE, Thambyayah M, Vigevano F, Wong V, Young C, Zhongshu Z.	Brain & Development 2001;23(7):441-738.
2002	Neuroimmunology and Childhood Epilepsies	Andermann F, Eeg-Olofsson O, Chiu SS.	Brain & Development 2002;24(8):788-795.
2003	Chromosomal Aberrations and Childhood Epilepsies	Andermann E, Battaglia A, Berkovic SF, Biraben A, Laan LEAM, Singhi P, Stephenson JBP, Wang P-J, Williams CA, Zuberi SM.	Brain & Development 2005;27(2):79-140.
2004	Neuronal Migration Disorders and Childhood Epilepsies	Battaglia GS, Crino PB, Curatolo P, Golden JA, Granata T, Guerrini R, Leventer RJ, Mochida GH, Otsubo H, Woermann FG.	Journal of Child Neurology 2005;27(2):79-140.
2005	Epileptic Syndromes in Infancy and Early Childhood	Andermann F, Berg AT, Capovilla G, Craiu D, De Vivo DC, Engel J Jr, Fejerman N, Hirsch E, Kasteleijn-Nolst Trenite DGA, Kim DW, Lee WL, Lux AL, Moshe SL, Nordli DR Jr, O'Regan ME, Plouin P, Sankar R, Scheffer I, Scher MS, Specchio N, Wolf P.	Epilepsy Research 2006;60 Suppl 1:S1-S279.
2006	Status Epilepticus in Infants and Young Children	Banu S, Fusco L, Kalra V, Lee JS, Lux AL, Neville B, Otsubo H, Sankar R, Shinner S, Specchio N, Wasterlain CG	Acta Neurologica Scandinavica Supplement 2007;115 Suppl 186

The 11th Annual Meeting of the Infantile Seizure Society

President: Yoshihiro TAKEUCHI
Professor and Chairperson, Department of Pediatrics
Shiga University of Medical Science
Shiga, Japan

Date: April 10-11, 2008

Venue: Royal Oak Hotel SPA & Gardens, Ohtsu (close to Kyoto)

Main theme: Febrile Seizures and Related Conditions

Objectives: Febrile seizures are the most common type of seizure experienced in childhood and provide a good example of the interaction between genetic susceptibility and environmental factors. Explorations thorough discussion on such issues as genetics, epidemiology, pathophysiology, imaging, subsequent epilepsy, mesial temporal sclerosis, treatment, education of febrile seizures and related conditions are in prospect.

Contact: The 11th ISS Secretariat
c/o Department of Pediatrics, Shiga University of Medical Science
Tsukinowa-cho, Seta, Ohtsu City, Shiga 520-2192, Japan
Phone: +81-77-548-2226 Fax: +81-77-548-2230
E-mail: iss2008@belle.shiga-med.ac.jp