International Symposium on Status Epilepticus in Infants and Young Children

Basic Mechanisms, Clinical Evaluation, Prognosis and Treatment

The 9th Annual Meeting of the Infantile Seizure Society

Program & Abstracts

Osaka; April 29 - 30, 2006

Ichou Kaikan Alumnus Union Building of Osaka University 2 – 2, Yamadaoka, Suita-city, Osaka, 565-0871, Japan

> Sponsored: Infantile Seizure Society (ISS), Japan

> > Co-sponsored:

Japan Foundation for Neuroscience and Mental Health

Supported:

Japan Epilepsy Society Japan Pediatric Society Japanese Society of Child Neurology

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WELCOME MESSAGES

Dear Colleagues;

I regard the holding of the International Symposium on Status Epilepticus in Infants and Young Children (ISSE) in Osaka, Japan as an honor and a privilege.

The symposium will focus on the 'Epileptic Status' of children and young infants. Although epileptic status has been an important theme within child neurology, the basic mechanism and treatment has not yet been fully established. Therefore, it seems only fitting that this topic is the primary focus of this international symposium. It is our hope that all participants will be able to share their knowledge and experience and gain a more thorough understanding of this subject.

Osaka has occupied an important position in Japanese medical history. European medical ideas and principles were introduced to Japan initially through 'Kaitokudo', an original school of the Faculty of Medicine, Osaka University, established in 1724.

So it is with a great sense of pride and expectation that I hope you will take the opportunity to see the many historical and interesting sites around Osaka.



Toshisature Naga-

Toshisaburo Nagai, MD, PhD, Prof. President of ISSE, Division of Child and Reproductive Health Area of Nursing Science, Course of Health Science, Osaka University, Graduate School of Medicine

Dear Colleagues and Friends

The Infantile Seizure Society proudly holds the 9th annual meeting in Osaka, Japan, from April 29 through 30, 2006. This is dedicated to a big event of the International Symposium on Status Epilepticus in Infants and Young Children (ISSE) - Basic Mechanisms, Clinical Evaluation, Prognosis and Treatment.

Since the first establishment in 1998, the Infantile Seizure Society adopted English as a unique official language with a belief that the Society could organize a truly meaningful meeting of world-wide scale only through a common communication media, that is, English. Science and medicine essentially are universal and borderless human treasures, for which our Society committed.

Thus, all meetings organized by the Society in the past were opened widely to the world; since 2001, in particular, the annual meetings were presented in the form of International Symposium concerning a single main theme. The theme heretofore dealt with include West Syndrome and Other Epileptic Encephalopathies in 2001, Neuroimmunology in 2002, Chromosomal Aberrations in 2003, Neuronal Migration Disorders in 2004, and Epileptic Syndromes in Infancy and Early Childhood in 2005. All these symposia had been very successful. The contents of presentations and discussions of respective symposium had been published in full in various authoritative journals.

The 9th annual meeting of the Infantile Seizure Society had chosen "Status Epilepticus in Infants and Young Children" as its main theme. There is no doubt that status epilepticus is one of the most serious and challenging acute CNS disorders. It is really fascinating to observe the explosion of new information in recent years concerning basic pathomechanisms and clinical knowledge of this potentially devastating disorder.

It is noteworthy here, however, that the advances took place recently mostly concern the subject of matured brain, but the study on developing brain remained rather scanty, in spite of enormous preponderance of the condition in early life.

We believe that the International Symposium 2006 in Osaka will offer a bulk of the latest knowledge on such specific issues of status epilepticus in infants and young children, to fill in a part, at least, of the possible defect existing in current information resources. We are sure that your attendance shall be scientifically rewarding and worth.

The season of April in Japan is one of the best. The surroundings are rich in historical treasures. An attentive, warm hospitality of Japanese society is already a world famous tradition. Therefore we are pleased to extend our heartfelt welcome to every colleague worldwide to the ISSE, Osaka, April 29-30, 2006.



Yukis Tikujana

Yukio Fukuyama, MD, PhD. Chairperson, The Infantile Seizure Society

Welcome Message by Council

On behalf of Osaka University Graduate School of Medicine, I would like to welcome you to Osaka, Japan.

Prof. Nagai, President of ISSE, has planned a stimulating Scientific Program incorporating recent advances in this field. I believe that a balanced representation of topics relating to basic sciences and clinical medicine has been achieved.

I believe that all the participants will have the opportunity of enjoying a high level Congress, but also the city of Osaka.

We are looking forward to greeting you in Osaka.



Masaya Johyama

Professor Masaya Tohyama, Dean, Osaka University Graduate School of Medicine

Positions:

Dean, Graduate School of Medicine, Osaka University. Professor and Chairman, Department of Anatomy & Neuroscience.

Editorial Board:

Molecular Brain Research, Brain Research, J. Chemical Neuroanatomy, Neuroscience Research, Pain

Membership:

Member of Directors, Japanese Neuroscience Society (1984~present) Member of Directors, Japanese Society of Pain (1988~present)

The Chief Director, Japanese Society of Neurochemistry (2004 \sim present)

Award:

Beltz Prize in Japan (1991)

Japan Bio Business Competition, The most valuable Prize(2000)

Highly Cited Researchers in Neuroscience by ISI (2001)

Japan Bio Business Competition, The valuable Prize(2004)

ORGANIZATION

Organizing Committee

[A] General

Supreme Ad	visor:	Yukio Fukuyan	na (Tokyo, Japan)
Chairperson	(President)	Toshisaburo Na	agai (Osaka, Japan)
Co-Chairper	rsons (Vice-presidents)	Shunsuke Ohta Kazuyoshi Wat	hara (Okayama, Japan) anabe (Nagoya, Japan)
Committee Members	Toshiaki Abe(Tokyo,Jap Tateki Fujiwara (Shizuo Mitsumasa Fukuda (Eh Shinichiro Hamano (Sai Shinichi Hirose (Fukuo Kazuie Iinuma (Miyagi, Masatoshi Ito (Shiga, Ja Tatsuro Izumi (Oita, Jap Osamu Kanazawa (Saita Mitsuhiro Kato (Yamag Ryutaro Kira (Fukuoka Jun Kohyama (Tokyo, Ja Toyojiro Matsuishi (Kur Hisao Miura (Kanagawa	pan) pka, Japan) ime, Japan) itama, Japan) ka, Japan) Japan) pan) pan) ama, Japan) ata, Japan) , Japan) rume, Japan) a, Japan)	Shin-ichi Niijima (Tokyo, Japan) Hirokazu Oguni (Tokyo, Japan) Akihisa Okumura (Tokyo, Japan) Yoko Ohtsuka (Okayama, Japan) Shinji Saito (Sapporo, Japan) Kenji Sugai (Tokyo, Japan) Yasuhiro Suzuki (Osaka, Japan) Satoshi Takada (Kobe, Japan) Takao Takahashi (Tokyo, Japan) Yoshihiro Takeuchi (Shiga, Japan) Hitoshi Yamamoto (Kanagawa, Japan) Tsunekazu Yamano (Osaka, Japan) Hideo Yamanouchi (Tochigi, Japan) Yasuko Yamatogi (Okayama, Japan)

[B] Scientific Program Committee

Chairperson	: Tsunekazu Yan	nano (Osaka, Japan)
Committee	Yukio Fukuyama (Tokyo, Japan)	Kenji Sugai (Tokyo, Japan)
Members	Masatoshi Ito (Shiga, Japan)	Yasuhiro Suzuki (Osaka, Japan)
	Hirokazu Oguni (Tokyo, Japan)	Satoshi Takada (Kobe, Japan)
	Shunsuke Ohtahara (Okayama, Japan)	Kazuyoshi Watanabe (Nagoya, Japan)
	Takeshi Okinaga (Osaka, Japan)	Hitoshi Yamamoto (Kanagawa, Japan)

[C] Fund Committee and Treasurer

& Treasurer: Toshisaburo Na	agai (Osaka, Japan)
Hisao Miura (Kanagawa, Japan)	Kiyoomi Sumi (Osaka, Japan)
Shin-ichi Niijima (Tokyo, Japan)	Tetsuzou Tagawa (Osaka, Japan)
Hirokazu Oguni (Tokyo, Japan)	Takao Takahashi (Tokyo Japan)
Takeshi Okinaga (Osaka, Japan)	Hitoshi Yamamoto (Kanagawa, Japan)
Kazumasa Ohtani (Wakayama, Japan)	Hideo Yamanouchi (Tochigi, Japan)
	& Treasurer: Toshisaburo Na Hisao Miura (Kanagawa, Japan) Shin-ichi Niijima (Tokyo, Japan) Hirokazu Oguni (Tokyo, Japan) Takeshi Okinaga (Osaka, Japan) Kazumasa Ohtani (Wakayama, Japan)

Sponsoring Organizations	
Sponsored:	Infantile Seizure Society(ISS), Japan
Co-sponsored:	Japan Foundation for Neuroscience and Mental Health
Supported:	Japan Epilepsy Society Japan Pediatric Society Japanese Society of Child Neurology
HEAD OFFICE	Toshisaburo Nagai, MD, PhD, Prof. Division of Child and Reproductive Health Area of Nursing Science, Course of Health Science, Osaka University, Graduate School of Medicine, 1-7, Yamadaoka, Suita-city, Osaka, 565-0871, Japan Tel & Fax: +81-6-6879-2531 Email:nagai-t@sahs.med.osaka-u.ac.jp

REGISTRATION

Desk for Registration and General Information, located at the entrance hall of Ichou Kaikan, Alumnus Union Building of Osaka University, will be opened for the following periods:

 April 29th (Saturday)
 08:15-18:30

 April 30th (Sunday)
 07:15-15:30

Pre-Registration

Those who completed the registration before Feburary 28, 2006, should go to the Pre-registrant Reception Desk, present his/her Registration Confirmation Sheet to the receptionist and then receive his/her ready-prepared bag.

■ On-Site Registration

Registration Form should be presented to the reception desk, after filling out its upper part only, together with the fee payment in Japanese yen (cash) of appropriate amount. The fee rates are defined variably as shown below according to the participant's category.

Regular participant	17,000 JP¥
ISS member	15,000 JP¥
AOCNA member	13,000 JP¥
Junior physicians*	15,000 JP¥
Accompanying person	Free
Grand Social Party	5,000 JP¥

ISS= Infantile Seizures Society,

AOCNA= Asian & Oceanian Child Neurology Association

*=Young physicians graduated from medical school after January, 2000. Students of post-graduate course are also applicable to this category.

■ To ISS members:

The members of the Infantile Seizures Society (ISS) are requested to pay his/her annual fees (\$3,000) at the registration desk. Any one who wish to become a member of ISS is requested to fill out the membership application form and pay the 2006 annual fee (\$3,000).

■ To AOCNA members:

The members of the Asian & Oceanian Child Neurology Association (AOCNA) are requested to contact with the AOCNA reception desk, and to confirm his/her correspondence address in the membership roster and status of his/her dues payment. To become a member of AOCNA, please fill out the application form and pay the two years fee for the year 2006 and 2007 (20.00US\$) or the whole life fee (100.00 US\$) in cash.

■ Don't miss the Grand Social Party

Please get together everybody in the Grand Social Party at the Restaurant Minerva, 2nd Fl, Ichou Kaikan on Saturday evening April 29th. It offers an ideal opportunity to meet with old as well as new friends, and to enjoy a world-famous traditional Japanese hospitality.

General Information

Date

April 29th (Sat) - April 30th (Sun), 2006

Venue

"Ichou Kaikan", Alumnus Union Building for Osaka University, 2-2, Yamadaoka, Suita-city, Osaka, 565-0871, Japan Phone : +81-6-6879-3548 URL:http://www.med.osaka-u.ac.jp/pub/general/alumni/intro.html

Inside the Building / Ichou Kaikan

Entire area of the 2nd and 3rd floor will be used for the ISSE. Oral presentations will be delivered at a single auditorium (Hankyu-Sanwa Conference Hall, 3rd floor), with a capacity of 250 seats. Posters will be exhibited at the Large Conference Room. Smoking is prohibited throughout inside the building. Participants are requested to wear the registration badge at all times.

Official Language

English. No simultaneous translation available.

Social Function

1) Presidential Welcome Reception

e: Friday, April 28 th , 7:00 pm - 9:00 pm
: The Room "Kouki", 3 rd floor, Hotel Hankyu Expo Park
Senri, Suita-city, Osaka
: Casual
: Limited to the invitees

2) Grand Social Party

Date & Time : Saturday, April 29th, 7:00 pm - 9:00 pmPlace: Restaurant Minerva, 2^{nd} floor, Ichou KaikanAttire: CasualAttendance: \Frac{1}{2}5,000 per person

Official Certificate for Attendance and CME Points

An official certificate for attendance at the ISSE will be delivered to all foreign participants.

To Japanese colleagues, a certificate for authorized CME units will be rewarded by two societies as follows:

Society	Attendance	Autho	rship
		Presenter	Co-author
Japan Pediatric Society	5 u	3 u	0 u
Japanese Society of Child Neurology	2 u	3 u	1 u

u= unit

Breakfast (once) and Lunches (twice)

A food service will be provided to attendees at the luncheon seminar, on both days, 29^{th} and 30^{th} , and also at the morning seminar of the day 30^{th} . Since a total number of food boxes is fixed, the provision is guaranteed for those attendees who submitted their reg-

istration forms to the ISSE Secretariat by April 15. For on-site registrants, a ticket will be provided for free of charge on the first-come first-win basis as far as they are available.

Coffee & Snack

Coffee and snack will be served at the 3rd floor, Ichou Kaikan.

Council Business Meeting

The council business meeting of ISS will be held at Restaurant Minerva, 2nd floor, Ichou Kaikan from 4:00pm to 5:30pm, April 30th, after the scientific program is over. The ISS councilors are requested to attend this meeting.

Satellite Business Meeting

The 3nd business meeting of the Pediatric Epilepsy Collaborative Study Group in Asia will be held at the Restaurant Minerva, 2nd floor of Ichou Kaikan, from 6:00 pm, on April 30th, Sunday. This is a semi-closed meeting but anyone who wishes to attend is encouraged to contact with Dr. Anannit Visudtibhan (Bangkok)

or Dr. Yukio Fukuyama (Tokyo)

by 5:00 pm, April 29th.

After this time limit, the attendance may be allowable, but a dinner service is not guaranteed.

"Golden Week"

A stretch of consecutive 9 days from April 29 (Sat) to May 7 (Sun) is called as "Golden Week", because everyday is a holiday during the period, except for isolated two working days of May 1st and 2nd. Public offices and banks will be closed. Money exchange either at the Airport or the hotel may be recommended. Tourism is popular nationwide. Shops and restaurants are mostly open.

Season

Deep spring season. Cherry blossom in Osaka area is usually over by April 15. Instead, an azalea and an iris will be flourishing. Weather is pleasant, moderately warm but not hot nor humid. Temparature ranged between 13° C to 25° C in average according to the past record.

Audio – Slides CD-R of the ISSE

Audio-Slides CD-R of the ISSE will be produced for educational purposes. It will contain almost all, except a few, lectures presented in the ISSE similar to the way they are presented by respective speakers. The majority of PC slides will be shown with synchronized oral presentations which are recorded on DVD. Quality of the CD-R will be excellent, because it will be produced by the Klub Class, Bangalore, India, which guarantees the best quality CD-R with global quality norms. We offer this CD-R at the ISSE participants' price of \$3,000 which includes mailing and handling costs. (\$5,000 for nonparticipants).

Please place an order with pre-payment in cash at the CD-R Order Desk.

Secretariat

■ Inquiries on ISSE 2006:

ISSE Secretariat: Toshisaburo Nagai, MD, PhD Division of Child and Reproductive Health, Course of Health Science, Area of Nursing Science, Graduate School of Medicine, Osaka University 1-7, Yamadaoka, Suita-city, Osaka, 565-0871, Japan Phone & Fax: +81-6-6879-2531 Email: nagai-t@sahs.med.osaka-u.ac.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/ISSE Website

http://www.iss-jpn.info/

HOTEL LOCATION AND VENUE ACCESS

1. Hotel List

0	Hotel Hankyu Expo Park	1- 5, Banpaku-koen, Senri, Suita city,
		Tel (06)6878 - 5151 ; Fax (06)6878 - 3456
	Nearest train station	Osaka Monorail : Banpaku Kinen Koen Sta.
•	Distance to the venue	ca. 25 min.
2	Hotel Mare Minami-Senri	1-2-D9, Tsukumo-dai, Suita-city,
		Usaka, 565-0862, Japan $M_{-1}(00)(2070, 1011, E_{-1}(00)(2070, 0000)$
	Nearest train station	1ei (06)6872 - 1911 ; Fax (06)6872 - 0062 Hankuu Bailway Sanni Lina : Minami Sanni Sta
	Distance to the venue	nankyu Kanway Senri Line : Minanii Senri Sta.
ß	Senri Hankvu Hotel	2.1 D-1 Shin-senri Higashimachi Toyonaka-city
U	Seni i Hankyu Hotei	Osaka 560-0082 Janan
		Tel (06)6872 - 2211 : Fax (06)6832 - 2161
	Nearest train station	Osaka Monorail : Senri Chuo Sta.
	Distance to the venue	ca. 30 min.
4	Toko City Hotel Shin-Osaka	2-32-9 Higashi Mikuni, Yodogawa-ku,
		Osaka, 532-0002, Japan
		Tel (06)6395-1515 ; Fax (06)6395-1516
	Nearest train station	Subway Midousuji Line : Higashi Mikuni Sta.
	Distance to the venue	ca. 40 min.
	Osaka Monorail Osaka Airport Senri Chuo Sta Subway Modusuji Higash Mikuni St	ISSE Vente Osaka * Univ. Handai Bvoin Mae Sta. Banpaku Kinen Koen Banpaku Kinen Koen Sta. Varrada Sta.
	Shin Osaka Sta.	ay Senti Line

2. Venue Access

<u>Ichou Kaikan</u> Alumnus Union Building of Osaka University

Address : 2 – 2, Yamadaoka, Suita-city, Osaka, 565-0871, Japan URL : http://www.med.osaka-u.ac.jp/pub/general/alumni/intro.html Phone : 06-6879-3548 (This is an outside line telephone number operating during the conference)

The convenient access to the ISSE venue are as follows ;

- A) Free shuttle bus services will be available to and from main hotels and the ISSE Venue, Ichou Kaikan.
- B) Handai Byoin Mae Station is a terminal station of Osaka Monorail Saito Line, from which it will take approximately 10 minutes walk to reach the Venue, Ichou Kaikan.

This map indicates a convenient walking route from Handai Byoin Mae Station to Ichou Kaikan, the Congress Venue.



3. Osaka Regional Map



INSTRUCTIONS FOR ORAL PRESENTATIONS

- 1. Keep the time as strictly as possible. Please note that the time frame shown in the program includes 5 min for discussion. A bell rings once to indicate one minute before the end, and twice in sequence to inform the time over.
- 2. Only one single projection will be available.
- 3. Every speaker is requested to finish up an arrangement necessary for data projection two hours before the respective presentation at the latest, by contacting with staff of the Data Preview Center, located at 3rd floor. Ichou-Kaikan.
- 4. The data has to be presented with USB flash memory or CD-R.
- 5. Facilities to preview are available at the Data Preview Center.
- 6. All presentations should be prepared by "PowerPoint, after ver. 2002" on Windows system. If your data was prepared by Mac system, the data may deform after its transfer to the Windows system. In this case, please check and correct this possible deformation at the Preview Center. If your PowerPoint is before ver. 2000, please inform it to the ISSE Secretariat by mail or to the staff of the Preview Center at the venue, as early as possible.
- 7. Each presenter is requested to manipulate the computer placed at the platform during the presentation. If you need help for manipulation, please inform to the ISSE Secretariat at the Preview Center. Your own personal computer is also available to use for presentation.
- 8. Video tape presentation is not available. If you need to use video records, please transfer them to the computer in a digital form. In this case, it is advised to bring your own personal computer, since the software does not fit often for your record. If you bring your own computer, Mac system is also available.

INSTRUCTIONS FOR POSTER PRESENTATIONS

- 1. Place: The Large Conference Room on the 3rd floor, Ichou-Kaikan.
- 2. Registration: The presenter is requested to register at the "Poster Reception Desk" placed at Preview Center.
- 3. Pushpins will be provided.
- 4. All presentations should be posted on the pre-assigned panel by 10:00 am, April 29th.
- 5. A poster panel has a surface of 90 cm wide and 180 cm high. Top space will be used to place the poster number in a size of 20 cm x 20 cm, pre-fixed by the Secretariat. The title, authors' names, and affiliations should be prepared by the presenters.
- 6. Poster round Presenters are requested to be present at the site of respective posters for discussion during the time of "Intermission & Poster Visit", 3:20pm- 4:30pm on April 29th. Poster visit is also scheduled during the time frame of "Lunch and Poster Visit" on both days, April 29th and 30th.

INSTRUCTIONS FOR DISCUSSION

- 1. Active discussion from the Floor is encouraged as far as the time is available.
- 2. All aspects of discussion session shall be ordered by due consideration of chairpersons.
- 3. Anyone who wishes to raise a question/discussion is urged to line up before the microphone stands to save a time, and wait for an order of chairpersons. To begin your discussion, please identify yourself first.

FLOOR PLAN

Ichou Kaikan

Alumnus Union Building for Osaka University

http://www.med.osaka-u.ac.jp/pub/general/alumni/intro.html



OVERVIEW OF DAILY PROGRAM

	Friday, April 28		Saturday, April 29		Sunday, April 30
7:00					
				7:15	Registration
8:00		8:15	Registration	8:00	Morning Seminar
		8:50	Opening Addresses		
9:00		9:00	Definition, Classification and Pathophysiology	9:10	Acute Encephalopathies 1
10:00		10:00	Epidemiology and	10:15	Aguto Enconhalopathios 2
			Management	10:45	Acute Encephaiopatilles 2
11:00		11:00			Prognosis
			Hippocampal Damages - Experimental Studies	11:45	Special Announcement
12:00			Enperimental States	11:55	
13:00		12:25	Luncheon Seminar (1) & Poster Visit		Luncheon Seminar (2) & Poster Visit
14:00		13:40	Hippocampal Damages - Clinical Studies	13:30	Panayiotopoulos Syndrome
15:00		14:10	Treatment 1	14:35	Neonatal SE
		15:20	T	15:25	Closing Address
16:00			Poster Visit	16:00	
17:00		16:30	Treatment 2		ISS Council Meeting
		17:35	Nonconvulsive SE	17:30	
18:00				18:00	
		18:25			
19:00 20:00	Presidential Welcome Reception (Invitees only)	19:00	Grand Social Party		Asian Pediatric Epilepsy Study Group Meeting
∠1:00					

PROGRAM

The 9th Annual Meeting of the Infantile Seizure Society

International Symposium on Status Epilepticus in Infants and Young Children (ISSE)

- Basic Mechanisms, Clinical Evaluation, Prognosis and Treatment -

Date: April 29th(Saturday) to 30th(Sunday)

Venue: Ichou Kaikan Alumnus Union Building of Osaka University, Osaka, Japan

PROGRAM – ORAL PRESENTATIONS

FIRST DAY, SATURDAY, APRIL 29

08:15 - 18:30 **REGISTRATION**

08:50 OPENING ADDRESSES

08:50 - 08:55

Opening address by Nagai T(President of ISSE)

08:55 - 09:00

Welcome address by Prof Tohyama M

(Dean, Graduate School of Medicine, Osaka University)

09:00 **Definition, Classification, and Pathophysiology**

Chairpersons: Sanker R (Los Angeles, USA) Takahashi T (Tokyo, Japan)

09:00 - 09:20

1 Definition and classification of status epilepticus <u>Osawa M</u> (Tokyo, Japan)

09:20 - 10:00

2 Advances in the pathophysiology of status epilepticus Wasterlain CG (Los Angeles, USA)

10:00 **Epidemiology and Management**

Chairpersons: Neville BG (London, UK) Sugai K (Tokyo, Japan)

10:00 - 10:20

3 A population-based epidemiological study of status epilepticus of children in Okayama, Japan

Ohtsuka Y, Nishiyama I (Okayama, Japan)

10:20 - 11:00

4 Management of convulsive status epilepticus in childhood Neville BG (London, UK)

11:00 Status Epilepticus and Hippocampal Damages-Experimental Studies **Chairpersons:** Wasterlain CG (Los Angeles, USA) Murashima Y (Tokyo, Japan) 11:00 - 11:15 5 Age- and dose-related hippocampal damage in the rat with kainic acid-induced status epilepticus Tokuhara D, Yokoi T, Sakuma S, Hattori H, Yamano T (Osaka, Japan) 11:15 - 11:45 6 Specific gene expressions before and after frequent seizures in the hippocampus of epileptic mutant EL mouse during development Murashima Y (Tokyo, Japan) 11:45 - 12:257 Inflammation exacerbates status epilepticus-induced injury in the developing rat brain Sankar R (Los Angeles, USA) 12:25 - 13:40 Lunch and Poster Visit 12:30 Luncheon Seminar 1 **Chairperson:** Niijima S (Tokyo, Japan) Sponsored by Kyowa Hakko Kogyo Co., Ltd, Japan 12:30 - 13:20 8 Epileptic encephalopathies: the main challenge for childhood epilepsy Neville BG (London, UK) 13:40 Status Epilepticus and Hippocampal Damages – Clinical Studies Chairpersons: Otsubo H (Toronto, Canada) Takeuchi Y (Shiga, Japan) 13:40 - 13:55 9 Hippocampal abnormalities after prolonged febrile seizures: a prospective MRI study Tanabe T, Hara K, Kashiwagi M, Shimakawa S, Tamai H (Osaka, Japan) 13:55 - 14:1010 Hippocampal volumes and diffusion weighted image findings in children with prolonged febrile seizures Natsume J (Nagoya, JAPAN) 14:10 Treatment 1 Chairpersons: Kalra V (New Delhi, India) Osawa M (Tokyo, Japan) 14:10 - 14:40**11** Treatment of convulsive status epilepticus in infants and young children in Japan

Sugai K (Tokyo, Japan)

14:40 - 15:00

12 Efficacy and safety of intravenous midazolam for status epilepticus in infants and toddlers: a retrospective multi-center study <u>Hayashi K</u>, Osawa M, Research Committee on Clinical Evidence of Medical Treatment for Status Epilepticus in Childhood (Tokyo, Japan)

15:00 - 15:20

13 Intranasal midazolam versus per-rectal diazepam as primary prevention against status epilepticus Kalra V (New Delhi, India)

15:20 – 16:30 Intermission (Coffee Break) and Poster Visit

16:30	Treatment 2
	Chairpersons: Specchio N (Rome, Italy) Ito M (Shiga, Japan)
	16:30 – 16:45
	14 Effect of intravenous infusion of lidocaine for status epilepticus in childhood
	Hattori H, Osawa M, Research Committee on Clinical Evidence of Medical
	Treatment for Status Epilepticus in Childhood (Osaka, Tokyo, Japan)
	16:45 – 17:05
	15 Malignant epileptic encephalopathy in infancy and its treatment with oral prednisolone.
	<u>Banu SH</u> ¹⁾ , Khan NZ ¹⁾ , Neville B ²⁾ (Dhaka, Bangladesh ¹⁾ ; London, UK ²⁾)
	17:05 – 17:35
	16 Magnetoencephalography for the surgical treatment of refractory status epilepticus
	<u>Otsubo H</u> (Toronto, Canada)
17:35	Nonconvulsive Status Epilepticus
	Chairpersons: Visudtibhan A (Bangkok, Thailand) Ohtsuka S (Okayama, Japan)
	17:35 – 18:05
	17 Is hypsarrhythmia an EEG pattern of nonconvulsive status epilepticus in infants? <u>Lux A</u> (Bristol, UK)
	18:05 – 18:25
	18 Clinical features of nonconvulsive status epilepticus in childhood
	<u>Inoue T</u> , Yasumoto S, Kanai N, Ogawa A, Tomoda Y, Ohfu M, Hirose S, Mitsudome A (Fukuoka, Japan)
19:00 -	- 21:00 GRAND SOCIAL PARTY
	Venue: Ichou Kaikan, Restaurant Minerva (2nd Floor)
	Participation : Registration required

15:30 REGISTRAT	ION
Morning Seminar	
 18:00 – 08:50 19 Effects of status Wasterlain CG (L 	Chairperson: Tanaka T (Asahikawa, Japan) epilepticus on brain development os Angeles, USA)
Acute Encephalop	oathies and Status Epilepticus 1
09:10 – 09:50	Chairpersons: Lux A (Bristol, UK) Hirose S (Fukuoka, Japan)
20 Acute encephalo <u>Mizuguchi M</u> , Yau (Tokyo, Tochigi, Y	pathies associated with influenza and other viral infections manouchi H, Ichiyama T, Shiomi M Yamaguchi, Osaka, Japan)
09:50 – 10:15 A proposal of ac (AEFCSE) and an on theophylline in <u>Shiomi M</u> (Osaka	ute encephalopathy with febrile convulsive status epilepticu n epidemic of AEFCSE in young Japanese children nedication , Japan)
Acute Encephalog	oathies and Status Epilepticus 2
Acute Encephalor	Dathies and Status Epilepticus 2 Chairpersons: Chi C-S (Taipei, Taiwan) Izumi T (Oita, Japan)
Acute Encephalog 0:15 – 10:30 2 Is theophylline a mortality in child <u>Maegaki Y</u> , Ohno	Dathies and Status Epilepticus 2 Chairpersons: Chi C-S (Taipei, Taiwan) Izumi T (0ita, Japan) risk factor for status epilepticus-associated morbidity and ren ? K (Yonago, Japan)
 Acute Encephalog 0:15 – 10:30 22 Is theophylline a mortality in child Maegaki Y, Ohno 0:30 – 10:45 23 First step therap Yoshikawa H (Series 1996) 	A chairpersons: Chi C-S (Taipei, Taiwan) Izumi T (Oita, Japan) risk factor for status epilepticus-associated morbidity and ren ? K (Yonago, Japan) y for status epilepticus during theophylline medication hdai, Japan)
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 Acute Encephalog 10:15 – 10:30 22 Is theophylline a mortality in child Maegaki Y, Ohno 10:30 – 10:45 23 First step therap Yoshikawa H (Seingen 1998) 10:45 – 11:25 24 Consequences of Shinnar S (New Yorks) 11:25 – 11:45 25 Prognostic facto Lee J¹, Seo J¹, Karson Special Announce 	Deathies and Status Epilepticus 2 Chairpersons: Chi C-S (Taipei, Taiwan) Izumi T (Oita, Japan) risk factor for status epilepticus-associated morbidity and ren ? K (Yonago, Japan) y for status epilepticus during theophylline medication ndai, Japan) Chairpersons: Shinnar S (New York, USA) Yamatogi Y (Okayama, Japan) f prolonged febrile seizures in childhood. Kork, USA) Kim HD ¹ (¹ Seoul, ²)Changwon, Korea)

Salonga AM, Ortiz HM (Manila, Philippines)

11:55 - 13:30 Lunch and Poster Visit

12:10	Lunch	neon Seminar 2	
	12:10 –	13:00 Chairperson: Ohtahara S (Okayama, Japan)	
	27 Wh	o is at risk for prolonged seizures ?	
	Shii	nnar S (New York, USA)	
13:30	Panayiotopoulos Syndrome and Status Epilepticus		
		Chairpersons: Fusco L (Rome, Italy)	
	13:30 -	14:00 <i>Oguni H (Tokyo, Japan)</i>	
	in ic	urrent autonomic status epilepticus without sequelae is a common event diopathic Panaviotopoulos syndrome	
	Fus	<u>co L</u> , Specchio N, Vigevano F (Rome, Italy)	
	14:00 –	14:20	
	29 Neu	29 Neuropsychological assessment of children with Panayiotopoulos syndrome	
	Spe	<u>Specchio N</u> , Fusco L, Masciarelli G, Vigevano F (Rome, Italy)	
	14:20 –	14:20 – 14:35	
	30 Clinical study on status epilepticus in Panayiotopoulos syndrome		
	Hira	ano Y, Oguni H, Hirano Y, Osawa M (Tokyo, Japan)	
14:35	Neonatal Status Epilepticus		
		Chairpersons: Salonga A (Manila, Philippines)	
	14:35 –	15:05 Watanabe K (Nagoya, Japan)	
	treatment protocols		
	Yan	namoto H (Kawasaki, Japan)	
	15:05 –	15:20	
	32 Midazolam in the treatment of neonatal seizures		
	Yan	nanouchi H, Kawaguchi N, Watabe Y, Imataka G, Nitta A, Suzumura H,	
	Egu	(Tochigi, Japan)	
15:25	CLOSI	NG ADDRESS	
	15:20 – Clos	15:30 sing remarks by Takahashi T (President, 10th Annual Meeting of ISS, 2007)	
15:30	ADJOL	JBN	
16:00 -	- 17:30	ISS COUNCIL MEETING	
		Infantile Seizure Society Council Meeting	
		Venue : Ichou Kaikan, Restaurant Minerva, (2 Floor)	
18:00 -	- 21:00	SATELLITE BUSINESS MEETING	
		Venue : Ichou Kaikan, Restaurant Minerva (2 nd Floor)	

Participation : Semi-closed

PROGRAM – POSTERS

Exhibition time: Day 1, April 29, 09:30 – Day 2, April 30, 13:30 Mounting: Day 1, April 29, 08:15 – 10:00 Take away: Day 2, April 30, 13:30 – 14:00

P 01 The influence of interleukin-6 on the propensity of hyperthermia-induced seizures in developing rats Fukuda $M^{1)}$, Shinonaga $C^{1)}$, Suzuki $Y^{2)}$, Kida $K^{1)}$, Morimoto $T^{1)}$ (Ehime¹⁾, Japan; New York²⁾, USA) P02 Dentate granule cell neurogenesis after pilocarpine-induced seizures in mice Kim DW¹, Lee KS² (Goyang¹ and Daejeon², Korea) P 03 The inhibitive effect of edaravon against kainic acid-induced neuronal cell death Shimakawa S, Miyamoto R, Tanabe T, Ogihara T, Tamai H (Osaka, Japan) P 04 Studies on oxidative stress in children with status epilepticus utilizing 8-hydroxydeoxyguanosine Fukuda M, Yamamoto H, Murakami H, Kamiyama N, Miyamoto Y (Kawasaki, Japan) P 05 Pathological characteristics of the focal dysplasia in children and experimental model Hodozuka A, Tsuda H, Hashizume K, Tanaka T (Asahikawa, Japan) P 06 Neurological and developmental outcomes following neonatal seizures Khongkhatithum C, Visudtibhan A, Thampratankul L, Chiemchanya S, Visudhiphan P (Bangkok, Thailand) P 07 Diagnosis and effective management of non-convulsive status epilepticus in Bangladeshi children Banu SH, Mawa J, Roy J, Mahbub M, Mosiul Azam AZM, Khan NZ (Dhaka, Bangladesh) P 08 Lowering of plasma valproic acid concentrations during concomitant therapy with meropenem in status epilepticus patients Ko TS, Yum MS, You SJ (Seoul, Korea) P 09 Propofol, a new treatment for pediatric refractory status epilepticus Shamsabad FM, Tonekaboni H, Ghofrani M, Armin S (Tehran, Iran) P 10 Efficacy of intravenous treatment of midazolam in children with status epilepticus Sakaue Y, Akahori S, Sawai T, Takikita S, Takano T, Takeuchi Y (Ohtsu, Japan) P11 High-dose steroid therapy for intractable localization-related epilepsy Nakata T, Suzuki M, Okumura A, Kato T, Hayakawa F, Ikuta T, Natsume J, Negoro T, Watanabe K (Nagoya, Japan)

P 12 Theophylline-related encephalopathy in childhood: Successful treatment with hypothermic therapy <u>Imakata G</u>, Miyamoto K, Mitsui M, Katashio H, Wake K, Yamanouchi H, Eguchi M (Tochigi, Japan)

P 13 Status epilepticus in Thai infants and children under age two: Etiology and response to initial treatment

<u>Thampratankul L</u>, Visudtibhan A, Khongkhatithum C, Chiemchanya S, Visudhiphan P (Bangkok, Thailand)

- P 14 Clinical characteristics and outcomes in children with status epilepticus as an initial seizure Kim MJ, Kim YO, Kim SH, Yi JS, Woo YJ (Gwangju, Korea)
- **P 15** Acute symptomatic seizures with or without status epilepticus in children $\underline{\text{Kim WS}}^{1}$, Lee EJ^{1} , Lee KS^{2} (Cheongju¹⁾ and Daejeon²⁾, Korea)
- **P 16** Prognosis of status epilepticus due to presumed encephalitis $\frac{\text{Kim KJ}^{1)}, \text{ Park SY}^{1)}, \text{ Hwang H}^{1)}, \text{ Chae JH}^{1)}, \text{ Hwang YS}^{1)}, \text{ Park HJ}^{2)}}{(\text{Seoul}^{1)} \text{ and Daejeon}^{2)}, \text{ Korea})}$
- P 17 The etiology and outcome of status epilepticus in children Ishii K, Matsuo M, Hamasaki Y (Saga, Japan)
- P 18 Outcome of encephalitis related severe refractory status epilepticus in children Lin JJ, Lin KL, Wang HS, Hsia SH, Wu CT, Chou ML (Taoyuan, Taiwan)
- $\label{eq:product} \begin{array}{l} \mbox{P 19} \\ \hline \mbox{Clinical study on status epilepticus in Dravet syndrome} \\ \hline \mbox{Sakauchi } \underline{M}^{1)}, \mbox{Oguni } H^{1)}, \mbox{Osawa } M^{1)}, \mbox{Hirose } S^{2)}, \mbox{Kaneko } S^{3)} \\ \hline \mbox{(Tokyo}^{1)}, \mbox{Fukuoka}^{2)} \mbox{ and Hirosaki}^{3)}, \mbox{Japan)} \end{array}$
- P 20 Electron transport chain complex IV deficiency patient with status epilepticus Kim SZ, Kim JM, Kang TY, Shin YO, Yoo T, Chung JH (Daejon, Korea)
- P 21 Atypical absence status epilepticus in one patient with cerebral folate deficiency Lee WT, Shen YZ (Taipei, Taiwan)
- **P 22** A case of cervical myelitis and cerebral vasculopathy caused by varicella-zoster <u>Choi JE</u>, Hong JN, Kim JH (Seoul, Korea)
- **P23** Refractory status epilepticus due to hemophagocytic lymphohistiocytosis Yano Y, Morimoto T, Fukuda M, Nakamura Y (Ehime, Japan)
- P 24 Acute encephalopathy with prolonged febrile seizure and late reduced diffusion (AESD)

 $\frac{\text{Takanashi J}^{1)}, \text{Oba H}^{2)}, \text{Barkovich AJ}^{3)}, \text{Tada H}^{4)}, \text{Yamanouchi H}^{5)}, \text{Kato M}^{6)}}{(\text{Chiba}^{1)}, \text{Tokyo}^{2)}, \text{Tochigi}^{4)} \text{ and Yamagata}^{6)}, \text{Japan ; San Francisco}^{3)}, \text{USA })}$

P 25 Prolonged febrile convulsion in children Sofue A, Natsume J (Aichi, Japan)

- P 26 Controversies in febrile convulsion Choedhury MA, Gupta G (Chittagong, Bangladesh)
- P27 Acute encephalitis with refractory, repetitive partial seizures: the presence of prolonged, peculiar inflammation
 <u>Saito Y</u>¹, Maegaki Y¹, Okamoto R¹, Ogura K¹, Togawa M¹, Nanba Y¹, Inoue T¹, Takahashi Y², Ohno K¹ (Tottori¹ and Shizuoka², Japan)
- $\begin{array}{c} \mbox{P28} \\ \mbox{Clinical study of 4 children of acute encephalitis with refractory repetitive partial seizures (AERRPS) with hippocampal lesion \\ \underline{Ohba~S}^{1}, Ishikawa~J^{1}, Togawa~M^{1}, Shiomi~M^{1}, Kuki~I^{1}, Okazaki~S^{1}, Ikeda~H^{1}, \\ \overline{Kawawaki}~H^{1}, Tomiwa~K^{1}, Takahashi~Y^{2} (Osaka^{1}) and Shizuoka^{2}, Japan) \end{array}$
- P 29 A case of acute encephalitis with refractory repetitive partial seizures accompanied with involvement of the basal ganglia

Miyata R, Motojima H, Mitsuiki N, Ishibashi N, Tomizawa E, Kohyama J (Tokyo, Japan)

P 30 MRI-diffusion weighted images of encephalopathy associated with human herpes virus 6

Araki A, Mori K, Takaya J, Kaneko K (Osaka, Japan)

Abstracts - Oral Presentations

DEFINITION AND CLASSIFICATION OF STATUS EPILEPTICUS

Makiko OSAWA

Department of Pediatrics, School of Medicine, Tokyo Women's Medical University, Tokyo, Japan

An appropriate definition and classification system for status epilepticus would improve communication among investigators and thereby promote research progress and ultimately better patient care. The WHO dictionary describes status epilepticus as 'a condition characterized by epileptic seizures that are sufficiently prolonged or repeated at sufficiently brief intervals so as to produce an unvarying and enduring epileptic condition'. Shorvon proposed that status epilepticus be defined as a condition in which epileptic activity persists for 30 minutes or more, causing a wide spectrum of clinical symptoms, and with highly variable pathophysiological, anatomical and etiological features. Such a definition would cover possible manifestations of status epilepticus.

Any true classification scheme must of necessity be provisional. Rigid adherence to a seizure type classification can lead to being overly restrictive, especially in terms of the status epilepticus observed in young children. A definitive classification of status epilepticus should not be based upon seizure type alone, relying on other features as well, the most important of which are patient age and the level of cerebral maturity, the pathophysiological mechanism underlying the epilepsy and clinical features. Status epilepticus in young children has not been well differentiated and its clinical manifestations in this population depend more on age than any other factor. The evolution over time of one type of status epilepticus into another as the child grows is further evidence of the relevance of cerebral development. To classify status epilepticus in early life, it is mandatory to focus on the importance of patient age and the level of cerebral development, as these are critical factors in defining the clinical type.

ADVANCES IN THE PATHOPHYSIOLOGY OF STATUS EPILEPTICUS.

Claude G. WASTERLAIN

Distinguished Professor of Neurology, Geffen School of Medicine at UCLA, West L.A. VA Medical Center, West Los Angeles, CA, USA.

Clinical status epilepticus (SE) is a diverse and heterogeneous condition, but several common features were noted as early as the 19th century: the very efficient mechanisms which normally terminate seizures fail during SE, seizures tend to become self-sustaining; and pharmacoresistance to benzodiazepines and other GAB-Aergic agents develops progressively. These features can be reproduced in animal models, and we are beginning to understand their mechanism. The transition from single seizures to SE is associated with GABA failure, and with internalization of the GABA_A receptors from synaptic membranes to endosomes, where they are inactive, and can be recycled to synapses or destroyed in lysosomes. The loss of potency of benzodiazepines seems to reflect a reduced number of γ 2-containing synaptic GABA_A receptors, as seizure-induced endocytosis progresses. At the same time, "spare" subunits of NMDA and

AMPA receptors are recruited to synaptic membranes where they form functional receptors, so that in some models responsiveness to NMDA antagonists improves with duration of SE. SE is also maintained by maladaptive changes in excitatory (substance P, neurokinin B) and inhibitory (galanin, dynorphin) neuropeptides. These processes offer potential targets for drug development, and have clinical implications: they offer a powerful rationale for pre-hospital treatment, which delivers drugs before benzodiazepine receptors are internalized. They suggest that benzodiazepines should be used in combination with an agent with a different mechanism of action, and that novel agents might target the trafficking machinery.

Supported by the Research Service of VHA, by grant RO1 NS 13515 (CGW) and by a KO8 award (JWYC) from NINDS

Abstracts - Oral Presentations

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A POPULATION-BASED EPIDEMIOLOGICAL STUDY OF STATUS EPILEPTICUS OF CHILDREN IN OKAYAMA, JAPAN

Yoko OHTSUKA, Itsuko NISHIYAMA

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

Background: Incidence of status epilepticus (SE) in Asian children, including Japanese, has not been reported.

Methods: We performed an epidemiological study of SE in Japanese children (<15 years of age) by ascertaining all first episodes of it in Okayama City in 2003.

Results: Thirty-six patients (22 males and 14 females) were identified. The incidence of SE was 37.6 per year per 100,000 population. Acute symptomatic etiologies were observed in 23 patients. Twenty-one of them were febrile illnesses, including influenza in 10. The other 13 suffered from epilepsy. The highest incidence (140.7/100,000) was seen in the age range of < 1 year, followed by those of 1-2 years

(87.0/100,000), and incidence became low after 8 years. This age-specific pattern was especially prominent in patients with acute symptomatic etiologies. In 25 of the 36 patients, SE was their first seizure. As for seizure types, 31 had convulsive SE, including tonic status in one. Five others showed nonconvulsive SE, including complex partial SE in four and absence status in one. No one died of SE. Two patients suffered from motor disturbance with or without mental disturbance after SE because of influenza encephalitis.

Conclusions: The incidence of SE was higher in Japanese children than in those reported in US Caucasians. The age-specific incidence pattern was similar in Caucasians and Japanese.

MANAGEMENT OF CONVULSIVE STATUS EPILEPTICUS (CSE) IN CHILDHOOD

Brian NEVILLE

Prince of Wales's Chair of Childhood Epilepsy, Neurosciences Unit, Institute of Child Health, London, UK

Status epilepticus is a serious complication or presentation of a seizure disorder in childhood. The incidence is about 20/100,000. Its management involves many issues.

- 1. Acute symptomatic patients account for the major mortality, particularly pyogenic meningitis in CSE with fever and a range of other conditions, metabolic, ischaemic and trauma including non-accidental injury. Thus diagnosis and management of cause is crucial.
- 2. Prophylaxis for those at risk is usually contingent and has to be planned.
- 3. Most episodes of CSE start in the community and require emergency management by carers or emergency services.
- 4. UK study showed that only 20% receive adequate initial treatment.
- 5. The same study showed a relationship between more than 2 doses of benzodiazepine

and respiratory depression.

- 6. The operational diagnosis of CSE for management is 5 minutes of seizure activity i.e. the length of a seizure that requires rescue treatment.
- 7. Several protocols exist for the management of CSE and cannot be easily compared. Two protocols, one for CSE in the Community and another for that occurring or presenting to hospital are required. When CSE has failed to respond to a third drug there is a high possibility of requiring intensive care.
- 8. The UK epidemiology study suggested intravenous lorazepam was preferable to rectal diazepam in Accident and Emergency Departments for those who have not received pre-hospital treatment and where first time treatment has failed i.v. phenytoin appears more effective than rectal paraldehyde. This was however not a trial of treatment.

AGE- AND DOSE-RELATED HIPPOCAMPAL DAMAGE IN THE RAT WITH KAINIC ACID-INDUCED STATUS EPILEPTICUS

Daisuke TOKUHARA, Toshiaki YOKOI, Satoru SAKUMA, Hideji HATTORI,

Tsunekazu YAMANO

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

Background: Immature brain is highly susceptible to seizures, but resistant to neuronal damage induced by status epileptics (SE). The mechanisms still remain unclear. This study was undertaken to elucidate them.

Methods: One to 8 week old Wistar rats were used for this study. Rats underwent SE induced by kainic acid (KA) were examined by immunohistochemistry and Western blot analysis.

Results:

- 1) SE was induced by lower dose of KA in the younger rats under 4-week-old than in adult-hood and didn't cause hippocampal damage.
- 2) Hippocampal BDNF levels were 5- and 3-fold higher in neonatal and adult rats at 1 day after SE than in each rats before SE, respectively.
- 3) Diazepam prevented hippocampal neuronal loss, if it suppressed SE under 30min. How-

ever, SE caused neuronal loss, if treated with diazepam 60 min later.

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- 4) Higher dose of KA induced a higher mortality rate and a shorter latency to the onset of SE.
- 5) KA dosage affected on the cell death mechanisms; KA (12mg/kg) induced necrotic neuronal death (TUNEL-negative, caspase-3 nondependent), whereas KA (9mg/kg) induced programmed cell death (TUNEL-positive, caspase-3 dependent).
- 6) Reactive astrocytes expressed estrogen receptor alpha (ERα) in the CA1 of the adult rats after SE. Glial expression of ERα may promote epileptogenesis after KA-induced SE.

Conclusions: Susceptibility and vulnerability to SE depend on age, KA dosage and SE duration. Treatment for SE should be based on those factors.

SPECIFIC GENE EXPRESSIONS BEFORE AND AFTER FREQUENT SEIZURES IN THE HIPPOCAMPUS OF EPILEPTIC MUTANT EL MOUSE DURING DEVELOPMENT

Yoshiya L. MURASHIMA, Jiro SUZUKI, Mitsunobu YOSHII

Department of Neural Plasticity, Tokyo Institute of Psychiatry, Tokyo, Japan

Background: Seizure activity is known to induce neurotrophic factor mRNA and protein expression. The level of neurotrophic factors in the hippocampus of EL mouse increases significantly after frequent seizures. In addition, the abundance of trophic factors could also facilitate the induction of cell division-related processes. Passage through the cell cycle is regulated by a family of cyclins that act as regulatory subunits for cyclin-dependent kinases (CDKs). The activity of various cyclin/CDK complexes regulates the progression of the cell cycle. In the present study, we used the EL mice to examine how the altered cyclin and the corresponding CDK family are related to the cell proliferation during development.

Methods: Developmental changes of cyclin family and corresponding CDK family (cyclin D/CDK-4, cyclin E/CDK-2, cyclin A/CDK-2, cyclin A/CDK-1, cyclin B/CDK-1) were examined during cell cycle by Western blotting in the hippocampus of EL mice and their control animal, DDY mice. Also, an attempt was made to identify the cell proliferation. by using systemic bromodeoxyuridine (BrdU) to label dividing cells. **Results:** Western blot analysis demonstrated a significant increase in the levels of cyclin B and

CDK-2 protein (G2/M checkpoint) in EL mice compared to the control DDY. These levels were increased predominantly after experienced frequent seizures. The number of BrdU positive cells in EL showed a significant increase after exhibiting frequent seizures.

Conclusions: The activation of cyclin and the corresponding CDK family complex is associated with the number of BrdU positive cells. It is concluded that in EL mice, during the development and particularly after repetitive seizures, reentry of cell cycle is promoted possibly because of the abundance of neurotrophic factors. DNA fragmentation without cell loss (Murashima YL et al, 2005 Epilepsia) and neuroneogenesis may work together in the processs of epileptogenesis during development.

INFLAMMATION EXACERBATES THE CONSEQUENCES OF STATUS EPILEPTICUS IN THE DEVELOPING RAT BRAIN.

Raman SANKAR^{1),} Stéphane AUVIN^{1, 2)}

- ¹⁾ Departments of Pediatrics and Neurology, David Geffen School of Medicine at UCLA, Los Angeles, CA, United States
 - ²⁾ Pediatric Neurology, Lille University Hospital, Lille, France

Background: Prolonged febrile seizures and status epilepticus (SE) have been implicated as predisposing factors for temporal lobe epilepsy and/or hippocampal sclerosis. We have previously shown an age specific pattern of neuronal injury following lithium-pilocarpine (LiPC) induced SE. Here, we assess the contribution of inflammation in the immature rat brain.

Methods: Rat pups of postnatal age 14 days (P14) were subjected to the lithium-pilocarpine model of SE. Lipopolysaccharide (LPS) was injected i.p., two hours prior to the induction of seizures: SE+LPS $50\mu g/kg$ (SE+LPS50), SE+LPS $100\mu g/kg$ (SE+LPS100), and control groups either received no LPS (SE group) or LPS $100\mu g/kg$, but no pilocarpine. Rats were killed after 24 hrs, and the brains examined for neuronal injury. Body temperature and duration of the SE were monitoring in both SE and SE+LPS100 groups. Finally, the number of epileptic animal in SE and SE+LPS50 groups were evaluated 3 month after the initial SE using

wireless EEG monitoring 24 hours a day during a 6 day period.

Results: SE resulted at 24 hours in 55.7 ± 12.9 injured neurons vs. 122.4 ± 19.6 in SE+LPS50 (p<0.05), and 159.2 ± 14 in SE+LPS100 (p<0.05). No eosinophilic neuron was observed in any of the LPS100 groups. No difference were found between SE and SE+LPS groups in both body temperature after the start of the SE and duration of the SE. In the long term study, 3/11 rats were epileptic in the SE group while 5/8 in SE+LPS50.

Conclusion: Inducing an inflammatory response exacerbates injury to the CA1 pyramidal cells and epileptic outcome. Presence of an inflammatory process could be a key variable accounting for the differences in vulnerability to seizure-induced injury between animal models and humans.

Supported by NINDS, NIH award NS046516 and AEAC Association (SA)

Luncheon Seminar 1

EPILEPTIC ENCEPHALOPATHIES: THE MAIN CHALLENGE FOR CHILDHOOD EPILEPSY

Brian NEVILLE

Prince of Wales's Chair of Childhood Epilepsy, Neurosciences Unit, Institute of Child Health, London, UK

Epileptic encephalopathy (EE) is the broad name given to alterations in functional state which are persistent but are regarded as a direct consequence of epilepsy rather than the causative lesion. EE is used to refer to both the state of the person suffering it and the pathogenesis. The majority of impairments associated with epilepsy are acquired either transiently or permanently by this process. It is poorly researched and it has been accepted that people with epilepsy have impairments which are present from early life but how they came by them is often ignored. This process results in a huge burden of disability and care and constitutes the main problem in epilepsy.

The impairments of EE are acquired with seizures or subclinical epilepsy, particularly with a high rate of seizure activity in sleep. All domains of functioning can be affected, including cognitive, behavioural, motor and visual. Within these domains, one can see arrest of developmental progress, loss of acquired skills or deviant patterns of development. Quite often, there is fluctuation of function which gives a clue to the pathogenesis. No change in magnetic resonance imaging has been reported using standard techniques but recently some more subtle changes are being reported. There is no change in head growth and patients may have the potential for recovery but are often left with major or minor deficits.

I exclude from EE the febrile status/mesial temporal sclerosis sequence, head trauma caused by seizures, Rassmussen's encephalitis and the effect of anti-epilepsy drugs. I will also pragmatically exclude epilepsy in patients with very severe primary brain damage or malformation such as lissencephaly and spastic tetraplegia because of the impossibility of assessing any change in developmental progress attributable to seizures. I also exclude the phenomena of the seizures themselves, the phenomena of transient cognitive impairment (ie. cognitive seizures), and transient post ictal phenomena, for example hemiparesis or aphasia. Such post ictal phenomena are however quite common in disorders and that cause encephalopathy, for example, Landau-Kleffner syndrome (LKS). I also exclude minor epileptic status in which the patient develops a groggy state with poor performance skills and impaired cognitive state but with observable myoclonic jerks and absences. This latter state could arbitrarily be regarded as an epileptic encephalopathy and often co-exists with a more long standing series of impairments. The reason for this exclusion is the presence of observable ictal phenomena i.e. there should not be any doubt that seizures are occurring.

Epileptic encephalopathies are common in early onset epilepsies and particularly in those starting up to the age of 6 months. They are usually associated with a high rate of epileptic discharges, particularly in sleep and they commonly have a poor response to routine anti-epileptic dugs. They constitute some of the major impairments that are associated with early lesions of the brain and our clinical task is to separate the effects of loss of eloquent cortex, downstream effects of cortical loss and those attributable to seizure activity.

The impairments that occur in childhood epilepsy consist of: seizures, cognitive arrest/regression, psychiatric illness (mood disorders, ADHD, autism, OCD) and motor disorders (apraxia, dystonia, ataxia).

They particularly occur in the severe early onset epilepsy syndromes which include the following:

- 1. early onset with hemimegalencephaly etc
- 2. Migratory focal epilepsy of infancy
- 3. early onset with right temporal dysembryoplastic neuroepithehal tumours
- 4. infantile spasms
- 5. Lennox-Gastaut Syndrome
- 6. Landau-Kleffner Syndrome
- 7. severe myoclonic epilepsy of infancy
- 8. Sturge Weber Syndrome

These usually have global effects upon cognition. LKS may produce a selective auditory agnosia, but may also produce more global cognitive and behavioural impairments.

Benign focal epilepsy with centro temporal spikes is commonly associated with a language processing disorder indicating that EEs may not all be severe.

The commonest of the regressive types of epilepsy is the syndrome of infantile spasms where the normal age of onset seizures is between 3 and 7 months and there is rapid developmental arrest and regression, particularly of visual responsiveness and communication and ultimately deviant development particularly along the autistic spectrum. Overall, 75-80% of children with infantile spasms suffer mental retardation, continuing epilepsy, and autistic spectrum disorder.

There is now accumulating evidence of temporal lobe dysfunction in the early onset severe epileptic regressions reported above. These include our right temporal lobe data linking both the dysembryoplastic lesions in the temporal lobe and the more general link between the right temporal lobe epilepsy of early onset and autism. Work on tuberous sclerosis has also indicated a higher rate of autism in association with temporal lobe tubers. The localisation of the EEG abnormality in Landau-Kleffner syndrome is very commonly in the temporal lobe and autistic features are commonly seen. Where Tuberous Sclerosis and autism coexist, FDG PET studies point to hypometabolism in the temporal lobe. We have studied event related potentials to novel stimuli in children with infantile spasms and demonstrated functional abnormality early in the course in the development of infantile spasms which points to a disturbance in the "wiring" within the temporal lobe which is compatible with a disorder localised to the posterior superior temporal gyrus. These responses are both delayed and blunted. This sort of phenomena may account for the permanent nature of much of the impairments that occur with this group of disorders despite apparently successfully stopping the seizures.

The epileptic encephalopathies, therefore, are a crucial part of our understanding and management of childhood epilepsy with many service implications. The latter includes the need for community based early ascertainment of epilepsy. We need clinical and neurophysiological systems for the early identification of deviant development. Motor disability assessment and management involving paediatric neurology, neurodisability, behavioural and psychiatric skills, psychology, therapy, specialist nursing and multiagency coordination are required, some of them are required for the person's whole life. In a sense, therefore, the seizures are not as important in childhood epilepsy as the accompanying encephalopathy and EEGs, particularly sleep EEGs in children with slow or deviant development, may be critical for our understanding of pathogenesis and management.
HIPPOCAMPAL ABNORMALITIES AFTER PROLONGED FEBRILE SEIUZRES: A PROSPECTIVE MRI STUDY

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Background: Whether prolonged febrile seizures (PFS) can cause hippocampal damage remains unclear. There have been few post-febrile seizure MRI studies.

Methods and Subjects: Two hundred and twenty-seven febrile seizure patients were admitted to Hirakata City Hospital between Feb 2004 and Jan 2006. Thirty-eight had PFS lasting over 15 minutes. Among them, 28 had MRI examinations and were enrolled in this prospective study. MRI was performed within a week of the seizure onset. Coronal sections perpendicular to the long axis of the hippocampal formation were obtained with T1, T2 and FLAIR images. MRI findings were independently evaluated by two pediatric neurologists and increased signal intensity on T2 and/or FLAIR image was judged to be clinically significant.

Results: Seizure duration was 15-30 min. in 8 cases, 30-60 min. in 19, 60-90 min in one. Hippocampal abnormalities with increased signal intensity were seen in only one of these cases, a one-year-old girl whose first febrile seizure manifested with ocular deviation to the right lasting 35 min. EEG revealed rhythmic ictal discharge in the left hemisphere associated with the seizure. High signal intensity in the left hippocampus was observed 72 hours later, followed by atrophic change 46 days after the event.

Conclusions: Our results suggest that PFS may cause hippocampal damage, although further follow-up is needed to reveal the causal relationship between PFS and mesial temporal lobe epilepsy with hippocampal sclerosis.

HIPPOCAMPAL VOLUMES AND DIFFUSION WEIGHTED IMAGE FINDINGS IN CHILDREN WITH PROLONGED FEBRILE SEIZURES.

Jun NATSUME

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Background: There is continued debate on whether status epilepticus can cause acute hippocampal damage, which could lead to mesial temporal lobe epilepsy. We assessed hippocampal volumes (HV) and diffusion weighted imaging (DWI) in patients with prolonged febrile seizures (PFS) and compared them with the seizure duration or EEG.

Methods: We studied 12 children within five days of a first episode of PFS. The hippocampus was segmented manually on MRI and signal intensity was evaluated visually on DWI. Seizure duration ranged from 40 to 95 minutes. In 7/12 patients, seizures lasted 60 minutes or longer despite intravenous infusion of diazepam. HV in patients were compared with those of 13 controls. HV abnormalities were correlated to seizure duration. DWI abnormalities were compared with HV, seizure duration and EEG abnormalities.

Results: The HV of patients were not significantly different from those of controls. However, when considering only patients with PFS for 60 minutes or longer, HV were significantly larger than in controls. In patients, there was a positive correlation between HV and seizure duration. DWI showed unilateral hippocampal hyperintensity in three patients with intractable seizures, and ipsilateral thalamic hyperintensity in two of them. EEG showed abnormalities on the side of DWI abnormalities.

Conclusions: Large HV and DWI abnormalities were seen in patients with intractable PFS. Our results suggest that medically intractable PFS may cause structural changes in limbic structures that could promote epileptogenesis.



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TREATMENT OF CONVULSIVE STATUS EPILEPTICUS IN INFANTS AND YOUNG CHILDREN IN JAPAN

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Background: Convulsive status epilepticus (CSE) is a life-threatening condition, particularly to infants and young children. In Japan, available IV drugs for CSE include diazepam (DZP), phenytoin (PHT), pentobarbital (PTB), thiopental (TP), and thiamylal (TA). Midazolam (MDL) and lidocaine (LDC) are widely used, but not officially approved, and IV form of lorazepam and phenobarbital (PB) are not available. We have proposed a guideline for treatment of CSE in children in Japan, based on EBM and consensus conference.

Summary points: When a patient has continuing seizures, IV DZP, 0.3-0.5 mg/kg, is given, however, if IV access is difficult, nasal or buccal MDL, 0.3 mg/kg, or rectal DZP, 0.5 mg/kg, is advisable. If seizures persist, IV MDL, 0.1-0.3 mg/kg, is given at 1 mg/minute, followed by DIV MDL, 0.1-0.15 mg/kg/hr with increase by 0.05-

0.1 mg/kg, up to 0.3 mg/kg/hr if seizures persist or relapse. When seizures continue, PHT, 18-20 mg/kg, is given at 1 mg/kg/hr. Finally barbiturates therapy is applied under respiratory and circulatory supports. IV PTB, TP or TA, 3-5 mg/kg, is given, followed by DIV PTB, 1 mg/ kg/hr with increase by 1 mg/kg/hr, up to 5 mg/ kg, or TH or TA, 2 mg/kg/hr with increase by 1-2 mg/kg/hr, up to 10 mg/kg/hr. Clustering seizures in benign infantile convulsions and convulsions with gastroenteritis do not respond to IV DZP, but excellently respond to oral carbamazepine (CBZ), 5 mg/kg, or IV LDC, 2 mg/kg, followed by DIV LDC, 2-4 mg/kg/hr, in case of vomiting. DZP and MDL are ineffective for theophylline-related encephalopathy and acute encephalitis with refractory, repetitive partial seizures, and early barbiturates therapy is recommended.



EFFICACY AND SAFETY OF INTRAVENOUS MIDAZOLAM FOR STATUS EPILEPTICUS IN INFANTS AND TODDLERS : A RETROSPECTIVE MULTI-CENTER STUDY

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Background: Recently, intravenous midazolam (MDL) was considered as effective treatment for status epilepticus (SE) and became popular choice in Japan. But there were no large population study to evaluate efficacy and safety of MDL therapy.

Methods: A retrospective multi-center study was carried out. The study subjects were 479 inpatients, from 1 month to 15 years old, who received intravenous MDL therapy for SE. From this population, patients in the age range from 1 to 23 months were chosen.

Results: 179 cases were enrolled. The underlying disorders were epilepsy in 75 cases, and acute symptomatic diseases in 104 (encephalitis or encephalopathy in 53 cases). MDL was ini-

tially administered as an intravenous bolus injection at a dose of 0.26 ± 0.22 mg/kg, and subsequently as a continuous intravenous infusion at a rate of 0.26 ± 0.28 mg/kg/hr. The intravenous bolus injection was effective in 73 (55.3%) of the 132 cases. In total, seizure suppression was obtained in 110 cases (61.5% of the total). Six patients died during the treatment period, but none of these deaths was associated with MDL therapy. The adverse events were consistent with previously reported data.

Conclusions: The present results indicate that MDL is an effective and safe drug for SE even in infants and toddlers, if used sufficiently early after seizure onset.

INTRANASAL MIDAZOLAM VERSUS PER-RECTAL DIAZEPAM AS PRIMARY PREVENTION AGAINST STATUS EPILEPTICUS

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Background: Prolonged seizures beyond 10 minutes may damage the brain and the need to intervene. Present study compares the efficacy of rectal diazepam (RD) vs intranasal midazol-am (MDZ) in prevention of status.

Methods: Randomized controlled single masked study, comparing intranasal MDZ (0.2mg/kg) and per-rectal diazepam (0.3mg/kg). Outcome measures included doctor to time & duration of seizure control, vital signs, adverse effects.

Results: 50 children, 200 seizure episodes, 100 per group studied. Baseline characteristics and seizure semiology were similar in both groups. Seizure types included GTCS, SPS, myoclonic/ infantile spasms and mixed seizures. Mean time to seizure control was 116.7 seconds in Mid-azolam vs 178.4 seconds in Diazepam group (p <0.005). Intranasal midazolam administration

was quicker to administer. Mean heart/ respiratory rate at 5,10 and 30 minutes was similar in both groups. Mean BP was lower in the DZ group though no clinically significant hypotension occurred. Mean SaO2 at 5 and 10 mins was lower after diazepam but returned to normal by 30 mins. In MDZ group, SaO2 remained normal. Efficacy determined by stoppage within 10 minutes was 88.3% in the PRD group vs 96.3% in the MDZ group ($p \le 0.09$).

Conclusions: MDZ is safe, convenient, easy medication at domiciliary level with therapeutic superiority over PRD in prevention of prolonged seizures ≥ 10 minutes.

We advocate use of intranasal MDZ in domiciliary setting status to prevent status epilepticus.

EFFECT OF INTRAVENOUS INFUSION OF LIDOCAINE FOR STATUS EPILEPTICS IN CHILDHOOD

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Background: Lidocaine has been used for the treatment of status epileptics (SE) in children. However, there have been no large, doubleblind, placebo-controlled studies of this treatment. This study examined the use of lidocaine for SE during childhood in Japan.

Methods: This was a retrospective multi-institutional study. Questionnaires were sent to 28 hospitals and data from patients admitted to these hospitals for SE and managed using lidocaine were included in the study. We enquired as to the patient background and the treatment and efficacy. Multivariate analysis was performed using SAS software.

Results: 261 cases of SE in patients aged one month to 15 years old were analyzed. SE was classified into continuous, cluster, and frequently repeated type. The usefulness of lidocaine was classified by examining the combination of its efficacy and adverse effects. Lidocaine use in 148 cases (56.7%) was evaluated as useful or extremely useful. Lidocaine was most useful in cluster and frequently repeated type SE and in the management of other acute illness such as infantile convulsion with mild diarrhea, whereas it showed poor effectiveness in CNS infection. The standard dose (around 2 mg/kg as an initial bolus, 2 mg/kg/hour maintenance) showed good outcome compared to lower and higher doses.

Conclusions: Lidocaine is useful for the management of SE in childhood. We recommend that lidocaine should be used for cluster or frequently repeated SE and other acute illness such as infantile convulsion as bolus injection of 2 mg/kg followed by continuous infusion of 2 mg/kg/hour.

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MALIGNANT EPILEPTIC ENCEPHALOPATHY IN INFANCY AND ITS TREATMENT WITH ORAL PREDNISOLONE

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Background: Large numbers of children presenting with seizures in hospitals have features of malignant epileptic encephalopathy (MEE) in infancy, ie, very early onset, multiple and high recurrence rate of seizures, with associated psychomotor developmental delay, whose seizures are difficult to control. In addition, they also have characteristic electroencephalographic (EEG) abnormality.

Clinical details: Within a period of six months 319 children with seizures attended the epilepsy clinic for the first time. Of them, 173 had characteristic electro-clinical features of MEE. A short course of prednisolone (PD) (1-2 mg/kd/day) was started on diagnosis. The preliminary

response was reviewed two weeks later. Eighty (58.4%) children had total, significant or some seizure control within 2 weeks of treatment, termed as "early positive responders", 19% had no remarkable seizure control, 10% had increased seizures. Three children (2.2%) had severe side effects. After one year of regular appropriate antiepileptic drug treatment majority of the children with positive response to PD treatment had significant seizure control.

Conclusion: Significant correlation was found between positive response to PD at 2 weeks and total seizure control after 1year regular follow up (p value <01).

MAGNETOENCEPHALOGRAPHY FOR THE SURGICAL TREATMENT OF REFRACTORY STATUS EPILEPTICUS

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Background: Refractory status epilepticus (RSE) is a life-threatening emergency that requires prompt treatment. Mortality in children with RSE treated with high-dose suppressive therapy (HDST) ranges from 16% to 43.5%. The surgical treatments have been reported for RSE in patients with pre-existing epilepsy. Magnetoencephalography (MEG) uses an equivalent current dipole model overlaid onto MR images to localize sources of interictal, infrequently ictal epileptiform discharges about epileptogenic zones. We report the value of MEG and surgical outcomes in the treatment of RSE.

Subjects: We studied four children (age: 2.5-10 years) who underwent video EEG, MEG and surgery for RSE. All patients failed initial HDST utilizing intravenous midazolam drip. MEG was performed under midazolam drip (2 patients). Three patients had pre-existing epi-

lepsy. Etiology was cortical malformations (3) and presumed encephalitis (1).

Results: Ictal dipole localizations were regionally concordant with ictal onset zones on scalp video EEG (2). Interictal MEG revealed unilateral clustered dipoles (3) and bilateral clusters (1). We performed cortical resections (2), functional hemispherectomy (1) and anterior temporal lobectomy (1). Status epilepticus stopped in all four patients. Two patients are seizure free at 3 years, 6 months follow up each. The other two have infrequent seizures.

Conclusion: MEG provides information of the epileptogenic zone for RSE. Ictal and interictal MEG data during status epilepticus can guide surgical resection to stop status epilepticus and avoid iatrogenic side effects associated with HDST.

IS HYPSARRHYTHMIA AN EEG PATTERN OF NONCONVULSIVE STATUS EPILEPTICUS IN INFANTS?

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Background: Hypsarrhythmia is generally associated with infantile spasms, a combination referred to as *West syndrome*. It is debatable whether hypsarrhythmia is usefully regarded as a form of nonconvulsive status epilepticus (NCSE).

Summary Points: The earliest English language description of hypsarrhythmia reported a "near-continuous" EEG pattern, although later studies showed a degree of state dependence. Its principal features are very high-amplitude, irregular slow-waves with superimposed multifocal epileptiform discharges. Paroxysms of spasms are clearly overt seizure events, and there are variable EEG patterns associated with this ictus. There remains debate about the definitional boundaries of hypsarrhythmia, and about the defining characteristics of NCSE. There is evidence that hypsarrhythmia is an age-dependent EEG pattern that evolves, sometimes independently of clinical features. Frequently, hypsarrhythmia is associated with delay in or regression of neuro-developmental skills, and recent studies have reported that a longer lead-time to diagnosis and effective treatment is associated with poorer long-term neuro-developmental outcomes. In many cases, adrenocorticotropin and corticosteroids act as apparent "rescue medications", with a relatively short treatment regimen having a sustained effect. The most effective antiepileptic drugs have predominantly GABAergic effects and might also be expected to be effective in NCSE. In the context of developmentally incomplete subcortical myelination and the presumably lower propensity during infancy for synchronisation of EEG discharges, these observations lend some support to the idea that hypsarrhythmia is an EEG pattern of nonconvulsive status epilepticus.

CLINICAL FEATURES OF NONCONVULSIVE STATUS EPILEPTICUS IN CHILDHOOD

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Purpose: To depict clinical features of nonconvulsive status epilepticus (NCSE) in childhood for early diagnosis and medical intervention.

Background: NCSE is as an epileptic condition lasting for 30 minutes or more without convulsion. The symptoms of NCSE in adulthood were well characterized and NCSE may account for about 25% of whole status epilepticus. In childhood, however, the fraction could be higher as NCSE may be overlooked given that children are unable to express their symptoms properly.

Methods: Medical history, ictal and interictal EEG, and the seizure symptoms were reviewed for five children with NCSE (3 boys and 2 girls: 1-10 years).

Results: The symptoms recognized as part of NCSE included strange behavior, sudden halt with blank appearance, falling down loosing

the strength and unstable gait. Lethargy, little speech, poor academic performance, loss of appetite and slow pace of eating were also recorded. Paroxysms on EEG were controlled in children who received diazepam during NCSE, and the clinical conditions were accordingly improved.

Discussion: Chief complaints of children with NCSE can be non-specific such as appetite loss or failure to thrive. When NCSE is suspected, one should take history carefully and perform EEG in combination with diazepam administration regardless of the presence of apparent convulsions.

Conclusion: NCSE should be on the list of differential diagnosis for children with behavioral problems even if the chief complaints appear irrelevant to epilepsy.





Morning Seminar

EFFECTS OF STATUS EPILEPTICUS ON BRAIN DEVELOPMENT

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Clinically and experimentally, the response of the developing brain to epileptic seizures and to status epilepticus (SE) is highly age-specific. There is a sharp distinction between infancy and childhood, and many degrees of variation within these groups. Neonates have a low cerebral metabolic rate and fragmentary neuronal networks limit seizure spread, so that they can tolerate relatively prolonged seizures without suffering massive cell death, but are vulnerable to seizure-induced changes in developmental plasticity. Experimental SE in neonates inhibits brain growth, modifies neuronal circuits, and can lead to behavioral deficits and to increases in neuronal excitability. Once past infancy, the developing brain is characterized by a high metabolic rate, exuberant neuronal and synaptic networks and overexpression of receptors and enzymes involved in excitotoxic mechanisms. Network maturation, however, is progressing but incomplete. A few areas of developmental vulnerability remain and match the domains of active maturation, such as myelination and the refinement of synaptic network connections. The effect of seizures on fine tuning of hippocampal place cells function (Liu et al, J Neurosci., 23:11505, 2003) is a case in point.

Seizure-induced neuronal loss: experimental evidence. SE induced in immature rats by kainate, pilocarpine, kindling, or flurothyl, show little or no neuronal loss, suggesting that some forms of status may not damage the immature brain. On the other hand, SE induced by kainate in immature rabbits or by perforant path stimulation, lithium/pilocarpine, or tetanus toxin in the immature rat brain reliably induce neuronal injury. Rats subjected to seizurelike perforant path stimulation on postnatal day 14-15 (P15), displayed specific loss of ipsilateral hilar interneurons with basket cell sparing. Lithium/pilocarpine SE in normoxic P10 rabbits showed massive hippocampal damage in a distribution resembling that observed in children dying during SE, and in mesial temporal sclerosis. The ontogeny of SE-induced neuronal loss (Sankar et al J Neurosci, 18:8382,1998) highlights its region- and age-secificity and the likelihood that it is the direct effect of seizure activity.

Seizure-induced neuronal loss: clinical evidence: Neuronal loss is seen in the brains of many patients with a history of febrile SE who come to surgery for intractable seizures. The association between prolonged convulsive episodes in childhood and mesial temporal sclerosis in patients with temporal lobe epilepsy has raised the question of causality. Prospective epidemiological studies have suggested a benign outcome of childhood SE (Maytal et al Pediatrics, 83:323,1989), although others show that seizure duration adversely affects prognosis. The presence of neuronal death in the brains of children dying acutely of status epilepticus is not conclusive, since it could be a result of the illness that cause the seizures, rather than a result of the seizures themselves. Among the factors that predict seizure recurrence, is a history of febrile seizures lasting over 15 min. MRI studies of the hippocampus in SE and in complex or prolonged febrile seizures anecdotally support a link between SE and mesial temporal sclerosis. In summary, experimental studies suggest many ways in which SE can adversely affect brain development, but clinical evidence is sparse,

ACUTE ENCEPHALOPATHIES ASSOCIATED WITH INFLUENZA AND OTHER VIRAL INFECTIONS

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Background: Acute encephalopathy is the most serious complication of pediatric viral infections, such as influenza. Every year, several hundreds of Japanese children are affected by influenza-associated encephalopathy. The mortality is high, and the survivors are often left with severe motor and intellectual disabilities, and with intractable epilepsy.

Summary Points: Acute encephalopathy is classified into three major categories. The first group caused by metabolic derangement consists of various inherited metabolic disorders and the classical Reye syndrome. Salicylate is a risk factor of the latter condition. The second group, characterized by a systemic cytokine storm (Ichiyama et al 2003) and vasogenic brain edema, includes Reye-like syndrome, hemorrhagic shock and encephalopathy syndrome, and acute necrotizing encephalopathy (Mizuguchi et al 1995). They may be aggravated by diclofenac and mephenamic acid. Severe cases are complicated by multiorgan failure and disseminated intravascular coagulation. The mortality is most high, although methylprednisolone pulse therapy may be beneficial in some cases. The third group, characterized by localized edema of the cerebral cortex, has recently been termed as acute encephalopathy with febrile convulsive status epilepticus (Shiomi 2000), and includes the hemiconvulsion-hemiplegia syndrome and acute infantile encephalopathy predominantly affecting the frontal lobes (Yamanouchi et al 2006). Theophylline may be a risk factor of these syndromes. The pathogenesis is yet to be clarified, but an increasing body of evidence points to excitotoxicity and delayed neuronal death.

A PROPOSAL OF ACUTE ENCEPHALOPATHY WITH FEBRILE CONVULSIVE STATUS EPILEPTICUS (AEFCSE) AND AN EPIDEMIC OF AEFCSE IN YOUNG JAPANESE CHILDREN ON THEOPHYLLINE MEDICATION

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Background: We proposed a new type of acute encephalopathy, "Acute encephalopathy with febrile convulsive status epilepticus (AEFCSE)", which is characterized by, sequentially, febrile convulsive status epilepticus (early seizure, ES), transient incompele recovery of 2-4 days duration, then repetitive afebrile focal convulsions (late seizure, LS) with neurological deterioration, and sequelae. CT shows localized cerebral edema, called as "lobar edema, LE" after LS. MRI-DWI shows high signals in subcortical white matter of affected lobes around 7 days of illness. The hemispheric type of AEFCSE is identical to hemiconvulsion-hemiparesis syndrome. But a distribution of LE is various in combination, such as bi-frontal, hemi-temporal, bi-frontal and hemi-parieto-temporal, etc. We investigate the probable triggers in 27 cases of AEFCSE.

Method and Results: In 11 AEFECS cases

theophylline was administered, with a recommended serum concentration except for one. Mean age of 11 theophylline cases is 33.1 ± 12.7 months and that of 16 non-theophylline cases is 15.4 ± 10.7 months (p<0.01). Infectious agents of non-theophylline cases were HHV6 (7), influenza (2), miscellaneous (5), unknown (2) and those of theophylline cases were influenza (2), HHV6 et al. (2), unknown (7).

Conclusion: Although in infants the precipitating factor of AEFCSE is viral agents common for febrile convulsion, in older children it seems to be therapeutic level of theophylline. Slow releasing theophylline powder is available only in Japan since 1995 and had been the most prescribed controller drug for childhood asthma until 2005 when Japanese Society of Pediatric Allergy and Clinical Immunology revised the asthma guideline.



9th ISS



IS THEOPHYLLINE A RISK FACTOR FOR STATUS EPILEPTICUS-ASSOCIATED MORBIDITY AND MORTALITY IN CHILDREN?

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Background: Status epilepticus (SE) is a common emergency in infants and children and poses a risk for SE-associated morbidity and mortality. We experienced some patients with SE during treatment for respiratory disease with theophylline administration followed by neurologic sequelae. In this retrospective study we sought to find risk factors including theophylline for outcome after SE during childhood.

Methods: Using multivariate regression analysis, we examined risk factors for fatality and neurological sequela after SE in children. Possible risk factors included sex, age at onset, the cause of SE, pyrexia, asthmatic attack during SE, past history of seizure, predisposing neurologic abnormality, seizure duration, type of seizure, and medication with theophylline. Consecutive patients with SE, aged 1 month to 18 years, who were referred to Tottori University Hospital from 1984 to 2002 were reviewed.

Results: Of 234 patients enrolled, 45 patients (19.2%) showed poor outcomes, namely acute death in 9 and neurological sequela in 36. The

cause of SE of acute neurologic insult and progressive neurologic disease was most significantly related to poor outcome (OR=33.68, P=0.000). We excluded 21 patients with the etiology of acute neurologic insult and progressive neurologic disease and then reanalyzed risk factors in the remaining 213 patients. Twenty-nine patients (13.6%) showed poor outcomes, namely acute death in 6 and neurological sequela in 23. Seizure duration of more than 2 hours (OR=12.73, p=0.000) and moderate to severe asthmatic attack (OR=31.61, p=0.010) were associated with poor outcome. Although, poor outcome was higher in patients with theophylline administration (11 of the 33 patients), but this was not statistically significant (OR=0.94, p = 0.951).

Conclusion: These results indicate that long lasting seizure activity and asthmatic attack would exacerbate SE-associated brain injury. Theophylline administration did not affect SE-associated brain injury in this study.

FIRST STEP THERAPY FOR STATUS EPILEPTICUS DURING THEOPHYLLINE MEDICATION

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9th ISS

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Background: A theophylline associated seizure (TAS) is considered a neurological emergency, as it is sometimes intractable and difficult to stop seizures with intravenous administration of diazepam. Therefore, the many patients who had status epilepticus during theophylline therapy need endotracheal intubation along with intensive cares, resulting in neurological sequelae. However, initial treatment for TAS have not been fully investigated.

Method: We compared the clinical features of 54 cases of TAS with those of 779 cases of non-TAS between 1991 and 2002, mainly centering on the therapy. Reports concerning with therapy for TAS were also reviewed.

Results: Among 54 cases, 47 patients (87%) were febrile, 36 cases showed generalized tonicclonic seizures and 18 cases of partial seizures. TAS occurred mainly in children under 3 years of age and the blood concentration of theophylline during seizures were within normal range in 78% of the cases. The duration of seizures lasted longer than that of non- TAS. The intravenous administration of diazepam was less effective to TAS (47%), compared with that to non-TAS (68%). Many cases needed repeated injection of diazepam, and fifteen cases (27%) resulted in endotracheal intubation. The efficacy of midazolam for TAS remains obscure. Nine cases had neurological sequelae.

Conclusions: Benzodiazepines, such as diazepam and midazolam, are known as the antagonist of theophylline, explaining its low effectiveness in TAS. In TAS, the use of other antiepileptic drugs such as barbiturates should be recommended promptly. This is to avoid brain involvements by the status epilepticus when diazepam is invalid. However, further study is necessary to establish effective and safe treatment for TAS.

CONSEQUENCES OF PROLONGED FEBRILE SEIZURES

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Introduction: Febrile seizures are the most common seizure type in childhood. While simple febrile seizures are benign, there is evidence that prolonged febrile seizures are associated with an increased risk of subsequent epilepsy, particularly temporal lobe epilepsy.

Methods: In a prospective study, we are prospectively enrolling children who present with febrile status epilepticus (>30min) and performing an MRI, EEG and viral studies within 72 hours. These studies are repeated at one year.

Results: To date we have recruited over 100 children. Mean seizure duration is 79min with approximately two thirds being focal. There is evidence of hippocampal injury (evidenced by

acute increased T2 signal) in approximately 30% including 10% with markedly increased T2 signal and 20% with milder signal abnormalities. EEG abnormalities including are also common, specifically focal slowing and attenuation. Approximately 40% have evidence of acute viral infection with human herpesvirus 6 or 7.

Discussion: The data provide evidence that acute hippocampal injury does occur in a significant proportion of children with febrile status epilepticus. The results of the one year MRIs are being analyzed. The cohort will be followed long term to determine whether the acute hippocampal changes are predictive of long term outcomes.

PROGNOSTIC FACTORS OF STATUS EPILEPTICUS IN CHILDREN

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Background: We studied prognostic factors such as neurologic sequelae and recurrence of SE in children.

Methods: We retrospectively reviewed the medical records of 259 children who were admitted to the Pediatric Neurology Department at Yonsei University College of Medicine with SE between April, 1994 and October, 2005. We analyzed the clinical findings and the relationships between age of onset, presumptive causes, types of seizure, seizure duration, recurrence, and neurologic sequelae.

Results: Relative incidences of generalized convulsive SE and non-convulsive SE were 75.7%, and 24.3%. Presumptive causes of SE were id-

iopathic in 36.7%, epilepsy in 36.7%, acute in 14.7% and remote symptomatic in 11.9%. Neurologic sequelae occurred in 25.8% and the mortality was 2.7%. Neurologic sequelae were lower in patients with idiopathic generalized convulsive SE (P<0.05). The recurrence of SE was lower in patients with an idiopathic etiology, an acute symptomatic epileptic etiology and the seizure duration less than 1 hour (P<0.05).

Conclusion: The neurologic outcomes and recurrence of SE were found to be associated with etiology, seizure type and seizure duration. Age and the presence of febrile illness were found to have no effect on outcome.





Luncheon Seminar 2

WHO IS AT RISK FOR PROLONGED SEIZURES ?

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Introduction: While most seizures are brief and self-limited, a subset are prolonged. Identifying children at risk for prolonged seizures may help in their management.

Methods: Risk factors for prolonged seizures were identified from several epidemiologic studies and review of the literature.

Results: Children with a prolonged first unprovoked seizure or a first febrile seizure do not have an increased risk of seizure recurrence. However, if the seizure does recur it is likely to be prolonged. In children with epilepsy, those at highest risk for prolonged seizures are those who experience a prolonged seizure early in the course of the disorder. Additional risk factors include young age of onset and remote symptomatic etiology or a progressive encephalopathy. Family history also plays a role as twins tend to be concordant not just for seizures but also for prolonged seizures. Those with prolonged seizures also tended to experience seizure clustering.

Discussion: There appears to be a subgroup of patients with a predisposition to prolonged seizures which appears to be independent of the tendency to have frequent seizures. This suggests a defect in the inhibitory mechanisms that cause most seizures to terminate quickly. These patients tend to declare themselves early in their clinical course

RECURRENT AUTONOMIC STATUS EPILEPTICUS WITHOUT SEQUAELAE IS A COMMON EVENT IN IDIOPATHIC PANAYIOTOPOULOS SYNDROME.

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Background: Clinical and experimental data suggest that prolonged seizures can have immediate and long-term adverse consequences especially on the immature and developing brain. Seizure duration of more than 30 minutes is considered dangerous as 30 minute of continuous epileptic activity causes loss of cerebral autoregulation.

Summary Points: Autonomic status epilepticus, that is the hallmark of Panayiotopoulos syndrome, always manifest itself with prolonged epileptic seizures with autonomic and motor signs. Seizures duration often exceeds 30 minutes, configuring a true status epilepticus, which in many cases requires intensive care unit. Despite this dramatic presentation, no children with idiopathic Panayiotopoulos syndrome present immediate or long-term sequelae. In our experience of 98 children with clinical and EEG features of Panayiotopoulos syndrome, the duration of first seizures was between 15 and 90 minutes. In 45% of children it was stopped by the administration of drugs in Emergency Room Department. Multiple seizures of same duration was observed in the following years in 35% of children. The follow-up is now between 1 and 14 years (mean 4 years). Recent neuropsychological investigations performed in 11 among 98 children have shown normal results. The question is: why status epilepticus in idiopathic epilepsy does not influence the cognitive development and does not produce short and long-term sequelae?

NEUROPSYCHOLOGICAL ASSESSMENT OF CHILDREN WITH PANAYIOTOPOULOS SYNDROME

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Background: Panayiotopoulos syndrome (PS) is a benign childhood disorder characterized by the recurrence of autonomic status epilepticus or prolonged focal seizure with autonomic symptoms. The aim of this study is to evaluate the signs of possible consequent cerebral damage in the follow-up, by a neuropsychological assessment.

Methods: Out of the 98 patients with PS, 11 subjects were randomly selected in order to administer a battery of age-appropriate neuropsychological tests, which explored the global cognitive level (WISC-R), attention (TEA-Ch), eye mindedness and verbal memory (TEMA), visual perception (TPV, Hooper VOT), motor coordination and praxias (VMI), language (Peabody, TROG, Boston Naming Test, FAS, Animal Naming). The main clinical character-

istics were: age at onset 2.8-7.5 years (m: 4.4y SD+1.3y); first seizure duration 35 minutes (15-60 minutes), sleep occurrence with all typical symptoms in 65%. Nine out 11 had antiepileptic drugs (CBZ, PB or VPA) for a mean period of 3 years. Interictal EEG showed occipital spikes only in 55% of patients.

Results: Neuropsychological evaluation revealed normal scores for most of the items, although a minimum and not statistical significant reduction in the attention and short term memory scores has been detected.

Conclusions: These results demonstrates a normal cognitive evolution in children with PS even with recurrent autonomic status epilepticus. The minimum reduction in some items has been considered to be an effect of the AED administration.







CLINICAL STUDY ON STATUS EPILEPTICUS (SE) IN PANAYIOTOPOULOS SYNDROME (PS)

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Background: We studied the clinical characteristics of SE in patients with PS to clarify that we can make a diagnosis of PS at the time of first SE.

Subjects and Method: The subjects were 69 children fulfilling the criteria of PS. We retrospectively analyzed the age at onset, clinical seizure manifestations, circadian rhythm, duration and associated factors to the first SE.

Result: Sixty-four of the 69 children (93%) experienced at least one SE during the clinical course. The onset age of SE ranged from 27 to 118 months (mean= 51). It started with either sudden vomiting or retching with eye-deviations followed by GTCS (n=37, 54\%), focal and

unilateral seizures (n=20, 29%), and prolonged consciousness disturbances only (n=12, 17%). SE developed during sleep in 42 (61%), awake in 8 (12%) and drowsiness in 13 patients (18%). It lasted 30~60 minutes in 33 (48%), 60~120 minutes in 16 (23%) and longer than 120 minutes in 17 children (25%). There were 17 children (25%) taking theophylline at the time of SE.

Conclusion: Sudden nocturnal attacks starting with vomiting or retching followed by prolonged motor seizures in normally developed children can lead to a suspicion of PS. The association of theophylline might be a promoting factor to prolong SE in PS.

NEONATAL STATUS EPILEPTICUS: DIAGNOSIS, CLASSIFICATION, RECOGNITION AND TREATMENT PROTOCOLS

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Background: Status epilepticus (SE) occurs in children of all ages. Recent epidemiologic investigations of SE show heightened morbidity and mortality in newborns and young infants. However, the definition of SE in newborns is not precise and not easily applied in clinical investigations or in clinical practice. To evaluate the underlying conditions, clinical features and treatment of SE in neonates, a retrospective multi-center study was performed.

Methods: In the initial investigation, questionnaires were sent to pediatric neurologists in 194 neonatal intensive care units of university hospitals, children's hospitals, and general hospitals in Japan. The questionnaires sought information on the background of each case, the types of seizures, etiology of SE, treatments, results and adverse effects of treatment for patients aged less than one week who had prolonged or frequently repeated seizures lasting more than 15 minutes and refractory to treatment with conventional anti-convulsants, such as diazepam (DZP), phenobarbital (PB) or phenytoin (PHT). As a secondary investigation, 65 cases which completely fulfilled these criteria were examined more fully.

Results: Subtle seizure followed generalized tonic seizures as the most frequent seizure types. Neonatal SE was most frequently associated with hypoxic-ischemic encephalopathy, followed by intracranial hemorrhage, central nervous system infections, and cerebral infarction. Midazolam (MDL), lidocaine (Lid) or pentobarbital were used for cases in which DZP, PB, and PHT were ineffective. Adverse effects of MDL and Lid were identified in 7.3% and 6.3% of patients respectively.

Conclusions: Probable neonatal seizures include electroclinical seizures, clinical seizures without ictal discharge and other nonepileptic movements, and the exclusion of nonepileptic seizures is important for appropriate treatment. MDL and Lid were useful drugs for the treatment of neonatal SE.



MIDAZOLAM IN THE TREATMENT OF NEONATAL SEIZURES

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Background: The two most commonly used medications for neonatal seizures (NS) are phenobarbital and phenytoin. Although many other antiepileptic drugs have been utilized, relative efficacy has not been sufficiently assessed. Objective of this paper is to evaluate the effectiveness and adverse events of midazolam in the treatment of neonatal seizures (NS).

Patients and Methods: Thirty-nine patients with neonatal seizure, who were admitted in the NICU of our hospital from 1996 through 2003. NS were provoked in 23 infants (60%) within 24 hrs after birth, and in 29 infants (74%) within 48hrs. The most common etiology for NS was hypoxia/ischemia (43%), the second intraventricular hemorrhage (13%).

Results: Midazolam was administered in 22

infants. Bolus IV was carefully done in 16 infants. NS disappeared in 4 infants (mean dose; 0.23 ± 0.10 mg/kg), decreased in 7 (0.15 ± 0.07 mg/kg), and unchanged in 5 (0.16 ± 0.14 mg/kg). Continuous IV infusion was done in 21 infants. NS disappeared in 7 (mean final dose; 0.33 ± 0.09 mg/kg/hr), decreased in 9 (0.34 ± 0.12 mg/kg/hr), and unchanged in 5 (0.36 ± 0.15 mg/kg/hr). Midazolam was judged as effective in 76% of infants with NS. No critical adverse event was seen. Most common adverse event was mild hypotension, which was found in 11 infants (28%), but controlled well with dopamine infusion.

Conclusions: Midazolam was effective and safe anticonvulsants for the treatment of NS.

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Abstracts - Posters

THE INFLUENCE OF INTERLEUKIN-6 ON THE PROPENSITY OF HYPERTHERMIA-INDUCED SEIZURES IN DEVELOPING RATS.

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Background: Previous studies indicated that several cytokines influence the seizure propensity in convulsive disorders and encephalopathies in childhood. We studied the role of one inflammatory cytokine, interleukin-6 (IL-6), in hyperthermia-induced seizures in developing rats.

Methods: Twenty-four male Lewis rats (23-28 days old) were divided into three groups (n=8 / IL-6 50ng, IL-6 500ng, and saline control groups). Two holes were made in the skull, one over the right frontal and one over the right occipital cortex, and silver screw electrodes for electroencephalography (EEG) were placed in them. We applied human recombinant IL-6 intra-nasally to developing rats 1h before seizures induced by moist heated air (50 degrees C). The seizure threshold was defined as the latency

from hyperthermia onset until the appearance of continuous seizure discharges on EEG, and the seizure duration was defined as the duration of continuous spike-and-wave discharges on EEG.

Results: The seizure threshold for the IL-6 (500ng) group, 360 (256-360) (median, range) sec, was significantly higher than that for the control one, 249 (121-360), (P<0.05). And the seizure duration for the IL-6 (500ng) group, 0 (0-20) sec, was significantly shorter than that for the control one, 33 (0-76), (P<0.025).

Conclusion: These results indicate that IL-6 plays an anti-convulsant role in hyperthermiainduced seizures in developing rats. Also, it is suggested that IL-6 has a neuro-protective effect on the developing brain.

DENTATE GRANULE CELL NEUROGENESIS AFTER PILOCARPINE-INDUCED SEIZURES IN MICE

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Background: Proliferation, differentiation, and survival of dentate granule cells have been reported to be influenced by epileptic seizures. This study was designed to investigate dentate granule cell neurogenesis after pilocarpine-induced seizures in mice.

Methods: Seizures were chemically induced by intraperitoneal injection of pilocarpine (300 mg/kg). Bromodeoxyuridine (BrdU, 50 mg/kg) was subsequently administered once a day for 6 consecutive days, starting at 24 hours after pilocarpine or saline treatment. Mice were sacrificed 24 hours after the last BrdU injection. We examined BrdU-positive cells by immunohistochemistry. To investigate the phenotypic pattern of newborn cells, the animals were allowed to survive for 28 days after the last injection of BrdU. We examined the long-term fate of BrdUpositive cells after seizures by double-labeled immunofluorescence with confocal microscopy.

Results: Quantitative analysis revealed that BrdU-positive cells were significantly increased in the pilocarpine-treated group compared to control $(230.55\pm59.50 \text{ vs.} 148.67\pm40.00, \text{ p}<0.05)$. The majority of these mitotic cells (92 %) were differentiated into neurons.

Conclusions: Our results indicated that mitotic activity in the dentate gyrus was enhanced after pilocarpine-induced seizures in mice, and the majority of all BrdU-positive cells showed the phenotypic differentiation to neuronal cells. POSTE



THE INHIBITIVE EFFECT OF EDARAVON AGAINST KAINIC ACID – INDUCED NEURONAL CELL DEATH.

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9th ISS

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Background: It has been already known that free radical scavenger inhibits neuronal cell death induced by kainic acid. But this neuro protective effect treated after the seizure status is not reported. 3 - methyl - 1 - phenyl - 2 pyrazolin -5 - one (edaravon) a newly developed free radical scavenger, has been applied clinically for cerebral infarction. We evaluate whether edaravon injected after kainic induced seizure status prevents kainic acid – induced neuronal cell death.

Methods: SD rats (160-180g) were used. Group 1 rats; Seizures were only induced by 10 mg/kg kainic acid injection. Group 2 rats; Seizures were induced by 10 mg/kg kainic acid injection and 30 mg/kg edaravon was given 3.5 hours af-

ter kainic acid injection. A week after this treatment, we compared the degree of cell survival in the hippocampus between these groups by Nissl stain and fluoro – Jade B stain.

Results: Edaravon didn't have an anticonvulsant effect. But it reduced kainic acid – induced neuronal cell death in hilus, CA3, and CA1.

Conclusions: As edaravon is a potent free radical scavenger and doesn't have an anticonvulsant effect, it may reduce cell death by the antioxidative effect. Because edaravon reduced cell death even if it is administered after seizure status, it is expected as a therapeutic drug against cell death in the hippocampus after seizure status, not only as a supplement.

POSTER 9th ISS

STUDIES ON OXIDATIVE STRESS IN CHILDREN WITH STATUS EPILEPTICUS: UTILIZING 8-HYDROXYDEOXYGUANOSINE

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Background: As a biomarker of DNA damage by oxidative stress, 8-hydroxydeoxyguanosine (8-OHdG) has been recently revealed to be a good candidate. Urinary and cerebrospinal fluid (CSF) levels of 8-OHdG were measured to estimate the contribution of oxidative stress to the disease state in children with status epilepticus (SE).

Methods: Urinary 8-OHdG levels were measured in 12 children (mean age: 36.3 ± 23.2 months) with SE and in 51 healthy children (mean age: 26.0 ± 20.5 months). The levels of CSF 8-OHdG were studied in 13 children (mean age: 39.3 ± 30.8 months) with SE. Subsequently, urinary and CSF levels of 8-OHdG were compared between children with SE and healthy children. The relationship between urinary and CSF levels of 8-OHdG was determined in 5 children where both urinary and CSF samples were

available. The measurement of 8-OHdG was conducted with an ELISA kit and a HPLC analyzer.

Results: The levels of urinary and CSF 8-OHdG in healthy children were 18.9 ± 8.50 ng/mg cre and 4.14 ± 2.06 pg/ml respectively. The levels of urinary (63.1 ± 99.6 ng/mg cre) and CSF (9.25 ± 3.08 pg/ml) 8-OHdG in children with SE were significantly higher than that of healthy children (p<0.01). A positive correlation between the levels of urinary and CSF 8-OHdG was noted in 5 children with both urinary and CSF samples available.

Conclusions: These results suggested that oxidative stress was strongly related to the acute brain damage in children. We disclosed that urinary and CSF 8-OHdG was a useful marker of oxidative stress in children with brain damage associated with SE.

PATHOLOGICAL CHARACTERISTICS OF THE FOCAL CORTICAL DYSPLASIA IN CHILDREN AND EXPERIMENTAL MODEL.

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Background: Cases of intractable epilepsy have been treated surgically, including focus resection. We have tried to identify the epileptic focus by using electrocorticography and to perform complete resection, but we have often observed epileptiform discharges also in perilesional areas such as the site of FCD.

Methods: Kainic acid solution was injected into the sensori-motor cortex of neonatal rats. Their behavior and EEG were recorded using a Video-EEG monitoring. Then, rats were perfused for pathological study. Fifteen surgical cases of FCD were subjected to the clinical study. Conventional EEG studies demonstrated focal epileptic phenomena. At surgery, electrocorticography was performed in order to localize epileptic foci. Pathological studies were performed.

Results: FCD was observed adjacent to the site

of the injection in all rats. EEG recording demonstrated focal spike discharges in and around the site of injection. Pathological studies showed decrease in GABA-A receptors and increase in GABA-B receptors not only in the lesion but also in perilesional areas. The immunohistochemical studies in clinical cases also showed decrease in GABA-A receptors and increase in GABA-B receptors in both the lesions and perilesional areas. These findings support the results of electrophysiological study.

Conclusions: In conclusion, not only the epileptic property of experimental focal cortical dysplasia but also perilesional epileptogenesis was demonstrated. In cases of FCD, total removal of the lesion and resection of the perilesional epileptic focus are needed for a good outcome.

NEUROLOGICAL AND DEVELOPMENTAL OUTCOMES FOLLOWING NEONATAL SEIZURES

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Background: Factors determining the outcomes of neonate with seizures are the underlying etiologies.

Method: A retrospective study was conducted to determine the outcomes of neonatal seizures from January 1993 to December 2002 at the Department of Pediatrics. The medical records of the neonates with any seizure within the first month of life were reviewed for eligible case. Collection of clinical presentation, results of physical examination, and laboratory findings were collected for descriptive analysis. Then, the children and their parents were invited for interview and physical examination.

Results: There were 61 neonates included into this study. More than one type of seizure was documented in 17%. Generalized tonic seizure was the most common type of seizure observed (39%). The other types of seizures were multifo-

cal clonic seizures (24%), subtle seizures (19%), focal clonic seizures (8%) and myoclonic seizures (3%). After initiation of treatment, 90% did not have seizure-recurrence. Hypoxic-ischemic encephalopathy was the most presumed etiology (30%). Association between poor neurological and developmental outcomes with asphyxia (OR 4.77, 95%CI 1.34 – 16.96) was observed. There was no association between the low birth weight and prematurity with the unfavorable outcomes. Two patients with severe asphyxia and one patient with primary brain tumor died during early neonatal period.

Conclusion: Etiology of neonatal seizures is the important prognostic factors documented in this report. Owing to limited data, it is not possible to emphasize the effect of seizures as the contributing factor of the concurrent brain injury.







9th ISS

DIAGNOSIS AND EFFECTIVE MANAGEMENT OF NCSE IN BANGLADESHI CHILDREN

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Background: Non-convulsive status epilepticus (NCSE) is an underdiagnosed neurological emergency. Its semiology and management pose some problems for clinicians. In our practice it was observed that recurrence of the status, despite standard treatment, was common. We started a protracted management of slow diazepam/midazolam infusion over 8 hours a day for three consecutive days, titrating the treatment with electroclinical evidences. The objective of this paper is to describe the efficacy of the treatment.

Clinical details: 7 children were diagnosed with NCSE in one year (from February 2005 to January 2006) at Dhaka Shishu Hospital. Regression of baseline psychomotor developmental skill was the common presenting feature in all of them. They were diagnosed and treated as per described protocol, which was followed by appropriate oral antiepilepsy drug (AED) treatment. After 8 hours infusion a day, repeat electroencephalography (EEG) was obtained on the next morning. Absence of characteristic EEG abnormality and return of the baseline psychomotor functional ability was achieved after treatment with 8 hours infusion for one day in 2, after 2 days in 2 and after subsequent 3 days in 3 children. Relapse of the condition was noted in one without oral replacement AED therapy 5 days after the IV treatment was stopped.

Conclusion: We propose a management protocol for NCSE in a hospital setting with slow infusion of diazepam or midazolam followed by appropriate oral AED replacement guided by close electroclinical monitoring.

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Background: Concomitant administration of meropenem has been reported to decrease the serum levels of valproic acid (VPA) in animals. But there are few reports in human. So we report 3 status epilepticus (SE) patients who were treated with VPA and meropenum concomitantly and whose serum levels of VPA decreased significantly.

Methods: We retrospectively reviewed the medical records of 3 SE patients who had experience that the level of VPA lowered during concomitant therapy with meropenem.

Results: Patients included were a 8-year-old male, a 7-year-old male, and a 15-year-old female respectively. All 3 patients had viral meningoencephalitis and SE. All 3 patients had taken VPA, all of whom had received other an-

tiepileptic drugs. The serum level of VPA decreased to the subtherapeutic levels during concomitant therapy with meropenem. Three of them returned to the therapeutic level after meropenem was discontinued. In one patient, the dose of valproic acid had to be increased by two times as much as the usual dose to maintain the therapeutic level. And two patients had more frequent seizure attacks when the serum level of valproic acid lowered.

Conclusion: These cases provided strong evidence for the interaction between VPA and meropenem. Therefore, physicians should be aware of this interaction that may be associated with the increase of seizure attacks as the results of the decreased level of VPA during concomitant therapy with meropenem.

PROPOFOL, A NEW TREATMENT FOR PEDIATRIC REFRACTORY STATUS EPILEPTICUS

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Background: Status epilepticus is a medical emergency, which necessitates prompt and aggressive treatment. The classical definition of refractory status epilepticus (RSE) describes a kind of seizure which does not cease in spite of sequential treatment of benzodiazepines, phenytoin and phenobarbital, or to a seizure continuing more than 60 minutes in spite of aggressive treatment. New antiepileptic drugs have provided alternatives to traditional treatment paradigms for RSE. Propofol is an intravenous anesthetic agent with a short duration of action. This drug can suppress central nervous system metabolic activity.

Methods: We tried to use propofol in the pediatric neurology department of Mofid Childrens' Hospital, Tehran, Iran, for treatment of RSE and compared its efficacy with midazolam. We recruited 32 patients with refractory status epilepticus. Of these 16 were treated primarily with midazolam and 16 received propofol.

Results: We achieved complete seizure con-

trol in 6 patients treated by midazolam (37.5%), whereas this was achieved in 10 of the 16 patients receiving propofol (62.5%). Complications in the midazolam group consisted initially of bradycardia, which led to cardiac arrest in one patient who fortunately recovered following cardiopulmonary resuscitation, and serum creatine phosphokinase elevation in another. Untoward reactions seen in the propofol group were characterized by serum creatine phosphokinase elevation in 5 patients and increases in the lipid profiles in another five (p=0.04) but in view of other complications such as apnea, hypotension, sepsis, electrolyte imbalance and median duration of stay in intensive care unit, no significant differences were seen.

Conclusions: We believe propofol, if used appropriately, can quickly and effectively terminate episodes of refractory status epilepticus. Also propofol terminated the seizures in higher numbers of patients than did midazolam.

EFFICACY OF INTRAVENOUS TREATMENT OF MIDAZOLAM IN CHILDREN WITH STATUS EPILEPTICS

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Background: Status epileptics is a medical emergency, and the adequate treatment is essential for a favorable neurological prognosis. In this study, the efficacy of intravenous midazolam was evaluated in pediatric patients with status epileptics.

Methods: Subjects consisted of 97 children (1 month to 16 years of age) with status epilepticus (108 seizure episodes), referred to the Shiga University of Medical Science from 1996 to 2004. The medical records of all patients were examined for details pertaining to epilepsy and drug approaches including midazolam administration.

Results: The etiologies of 108 seizure episodes were as follows: epilepsy in 50, febrile convul-

sion (FC) in 37, and acute encephalopathy/encephalitis in 10. In epilepsy group, the duration of status epilepticus was significantly short in patients with midazolam treatment compared with those without midazolam administration. The rate of seizure cessation was significantly higher in patients with midazolam than those with diazepam treatment in epilepsy group. Adverse effects of midazolam were recognized in only one patient showing transient hypoxemia, but mechanical ventilation was not required.

Conclusions: Administration of intravenous midazolam is suggested to be one of the most effective treatments for status epilepticus in children.







HIGH-DOSE STEROID THERAPY FOR INTRACTABLE LOCALIZATION-RELATED EPILEPSY

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Background: It is generally accepted that steroids are effective against some kind of localization-related epilepsy (LRE), such as epilepsy with continuous spike-waves during slow wave sleep. However, there have been few studies whether steroids are effective against other types of intractable LRE. We report 2 patients with intractable LRE whose clustered seizures were successfully treated with high-dose steroids.

Clinical Details: Patient 1 was a 3-year-old girl with severe mental retardation who had been treated for LRE since 2 years of age. She had complex partial seizures in cluster. Although she was treated with several antiepileptic drugs, her seizures persisted. Continuous intravenous infusion of thiamylal followed by oral high-dose phenobarbital succeeded in stopping seizures. Brain MRI showed diffuse atrophic changes during the course. Three months later, clustered seizures recurred, but were successfully controlled with intravenous methylprednisolone (30 mg/kg for three days). Case 2 was an 11-year-old girl with frontal lobe epilepsy. She had clustered seizures refractory to first-line antiepileptic drugs. Her seizures were controlled by continuous intravenous thiamylal. However, clustered seizures recurred after discontinuation of thamylal. MRI showed new high intensity areas in the right temporal lobe on T2weighted images and FLAIR. Her seizures were successfully treated with high-dose methylprednisolone.

Conclusions: High-dose steroids may have a beneficial effect in some patients with intractable LRE refractory to first-line antiepileptic drugs, and can be an option of treatment for intractable LRE.



THEOPHYLLINE-RELATED ENCEPHALOPATHY IN CHILDHOOD: SUCCESSFUL TREATMENT WITH HYPOTHERMIC THERAPY

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Background: The convulsion and the disturbance of consciousness are the most serious adverse effects of theophylline. It may provoke status epilepticus as well as prolonged coma, leading to a theophylline-related encephalopathy. This situation is usually encountered in children less than 6 years, and is resistant to anticonvulsants. Serum level of theophylline usually is not exceeded over optimal level. Severe neurological sequelae frequently follow.

Clinical Details: This 4-year-old girl was admitted for status epilepticus with hyperpyrexia. She had taken theophylline and one episode of febrile convulsion. The convulsion did not cease by conventional anticonvulsants and persisted for 90 min. She was diagnosed as acute encephalopathy, which might be related with theophylline intake. Serum level of theophylline was 7.0 μ g/dl. Pyridoxal concentration was decreased.

In CSF, IL-6 was elevated up to 92.7 pg/ml. EEG showed poorly synchronized high-voltage slow waves. Mild hypothermic therapy and methylprednisolone pulse therapy were undertaken. Intravenous administration of pyridoxal phosphate was also done. At 18th day, 99m-ECD SPECT showed asymmetrical decreased perfusion at the frontal lobes. MRI exhibited mild atrophic changes in the cerebrum. At the 28th day, she never spoke words and IQ test scored 16. At 10 months after the onset, her IQ scored 87, and SPECT presented improved cerebral perfusion.

Conclusions: We suggest that mild hypothermic therapy in combination with methylprednisolone pulse therapy and pyridoxal phosphate may be a candidate for the treatment modality against theophylline-related encephalopathy.

STATUS EPILEPTICUS IN THAI INFANTS AND CHILDREN UNDER TWO: ETIOLOGY AND RESPONSE TO INITIAL TREATMENT

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Background: Factors determining the outcome of status epilepticus (SE) include age of the patients, etiology, and duration of seizure. There is no report in the country addressing the response to initial treatment to the etiology in young children in Thailand. Therefore, a study of this condition will lead to appropriate treatment for Thai children.

Methods: Medical records of infants and children younger than two years admitted to the Department of Pediatrics with the diagnosis with SE from 1998 to 2005 were reviewed. Underlying diseases, precipitating factors, duration of seizure, laboratory results, response to initial treatment and clinical course were collected for descriptive analysis.

Results: There were 9 boys and 1 girl (agerange7 days -23 months, median 10.25 months) included in the study. Five patients had epilepsy prior to the onset of SE. There were 4, 4, and 2 patients categorized into cryptogenic, acute symptomatic and remote symptomatic respectively. SE in six patients was associated with acute febrile illness. Seizure was successfully terminated in 4 patients with treatment with intravenous sodium valproate and phenobarbital. Seizures in four were refractory to extensive treatment including intravenous midazolam and xylocard. Three of these children had cryptogenic cause. SE was partially controlled in the other two who had severe sepsis and severe bacterial gastroenteritis.

Conclusion: SE in children with cryptogenic cause or acute infection had unfavorable response to treatment. Febrile illness was the most common precipitating factor of SE in infants and young children under two.

CLINICAL CHARACTERISTICS AND OUTCOMES IN CHILDREN WITH STATUS EPILEPTICUS AS AN INITIAL SEIZURE

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Background: To determine the morbidity and mortality of children with status epilepticus (SE) as an initial seizure and to compare this in children under and over 2 years.

Methods: The 78 cases $(38 < 2 \text{ years and } 38 \ge 2 \text{ years})$ with SE as an initial seizure admitted to Chonnam National University Hospital between Jan 2000 and Jan 2004 were reviewed. **Results:**

- 1) SE as an initial seizure occurred predominantly in children less than 5 years old.
- 2) Febrile causes were the most common in children under 2 years, whereas acute symptomatic causes were most common in those over 2 years (P<0.05).
- 3) Generalized tonic-clonic seizures were the most common type.

- 4) The mortality rate was 6.4% (5 cases: 1 < 2 years and $4 \ge 2$ years).
- 5) The estimated occurrence of epilepsy after SE was 24.4% (19 cases: 8 cases < 2 years and $11 \ge 2$ years).
- 6) Neurologic sequelae after SE in cases that had developed normally before SE (62 cases: 32 < 2 years and $30 \ge 2$ years) were observed in 20 cases (32.3%), and were more frequent over 2 years (21.9% vs. 43.3%)(P<0.05).

Conclusions: In this study, death was less common and the neurologic sequelae of initial SE were less severe in children under 2 years of age. The cause seemed to be the difference in the etiology of SE with age.





ACUTE SYMPTOMATIC SEIZURES WITH OR WITHOUT STATUS EPILEPTICUS IN CHILDREN

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Background: Acute symptomatic seizures differ from epilepsy in that they have a clearly identifiable proximate cause and they are not characterized by tendency to recur spontaneously. But we hypothesized that acute symptomatic seizures with status epilepticus (SE) have an increased risk of subsequent seizures than those without status epilepticus.

Methods: We retrospectively studied five hundred and twelve children with seizures visited our hospital from January 1998 to December 2003. Among those children, 167 patients were determined as provoked seizures, and the patients were followed up for 2 years.

Results: One hundred and nine children had acute symptomatic seizures. The ages of first seizures were 1.58 ± 2.53 years. Causes in order of frequency were acute gastroenteritis (31.0%), minor infections (23.9%), CNS infections (7.0%),

encephalopathy (7.0). At two year follow-up, the incidence of the unprovoked seizure was 31.1% for children with acute symptomatic seizures. The risk of the unprovoked seizure was significantly greater for children with acute symptomatic seizures with SE (56.3%) than those without SE (25.2%).

Conclusions: The leading cause of acute symptomatic seizures was acute gastroenteritis. The incidence of subsequent unprovoked seizures was highest in the group of encephalitis/encephalopathy. The risk for subsequent unprovoked seizures was greater for those with SE than those without SE. The risk of subsequent unprovoked seizures is determined by underlying precipitation factors. Children with acute symptomatic seizures with SE should be followed up carefully.

OSTER PROGNOSIS OF STATUS EPILEPTICUS DUE TO PRESUMED ENCEPHALITIS

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Background: Encephalitis is a major cause of status epilepticus (SE) in children. This study was performed to investigate the clinical features and prognosis of SE due to presumed encephalitis.

Methods: Among the 138 patients who had presumed encephalitis, 25 children (16 male and 9 female) with SE were reviewed.

Results: The age at the onset of SE ranged between 1.1 and 13 years (mean 5.9 years). Twenty two patients presented with high fever prior to the onset of seizures. Twenty four patients showed altered mentality or behavioral change. Initial EEG showed abnormal background activity in all of the twenty one patients: diffuse slowing in 19 and diffuse suppression in 2. The duration of SE was within 24 hours in 5 patients, less than 10 days in 10 patients and 10 days or more in 6 patients. Ten patients were refractory to first line anticonvulsants (phenobarbital and phenytoin with or without valproate). Seventeen children continued to suffer from seizures, and seizures were intractable in thirteen of them. Cognitive sequelae were present in seventeen children, and four of them were in bed-ridden state. Follow-up brain MRI showed abnormal findings in sixteen patients: diffuse atrophy in 10, hippocampal sclerosis in 4 and encephalomalacia in 2.

Conclusions: The severe refractory SE owing to encephalitis carries a poor morbidity in terms of seizures and cognition at follow-up.

THE ETIOLOGY AND OUTCOME OF STATUS EPIELPTICUS IN CHILDREN

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Background: Status epilepticus (SE) is a common pediatric emergency. This study was conducted to determine the etiology and outcome of SE in children.

Methods: We retrospectively reviewed the medical records of 111 patients with SE who admitted to our hospital between 1987 and 2001. The patients were aged one month to fifteen years (mean, 3.49 year-old), and 18 of them had recurrent SE. Telephone questionnaires were used to know the outcome of 99 patients.

Results: The etiologies of febrile SE (74 patients) consist of 50 patients with febrile seizures (Fs), 3 with idiopathic epilepsy, 12 with symptomatic epilepsy, and 4 with encephalitis/

encephalopathy. Whereas, nonfebrile SE (37 patients) consists of 13 patients with idiopathic epilepsy and 13 with symptomatic epilepsy. Diazepam was effective among 68 episodes (59.6%) of SE, but intravenous barbiturate was needed for 14 episodes (12.2%) of SE. Recurrence of seizures occurred in 16 patients (36.4%) with Fs and 33 patients (84.6%) with epilepsy. The duration of seizure did not correlate with the neurological sequelae. The outcome was almost good in Fs, but poor outcome was observed in symptomatic epilepsy and encephalitis/encephalopathy.

Conclusions: The prognosis of SE depended not on SE itself but on the etiology.

OUTCOME OF ENCEPHALITIS RELATED SEVERE REFRACTORY STATUS EPILEPTICUS IN CHILDREN

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Background: Refractory status epilepticus (RSE) is the persistence of seizure activity despite appropriate therapy. It is treated with high-dose suppressive anesthetic agents. We report here the outcome of encephalitis related RSE in children in our hospital.

Methods: From Feb 2005 to Dec 2005, a retrospective chart review was carried out in the pediatric intensive care unit of Chang Gung Children's Hospital, and 8 children (ages 2year 2 month to 14year 5 months) with encephalitis complicated with refractory status epilepticus were enrolled in this study. The clinical characteristics were systematically assessed. Burst suppression coma was induced by high-dose suppressive therapy consisting of Deparkine, midazolam, lidocaine, propofol infusion, or high-dose phenobarbital. 24hr EEG monitor was performed in each patient. The goal of treatment is to achieve complete control of clinical seizure or burst-suppression pattern on

EEG, aiming for an interburst interval of >5 s. Brain MRI was followed after stable condition. The neurological evolution was scored in terms of motor function, cognitive function, and seizure disorder.

Results: Of the 8 patients, all (100%) children presented with fever several days prior to the onset of seizures and consciousness disturbance. 6 (75%) had vomiting and 3 (37.5%) had head-ache. In etiology, 3 were Mycoplasma pneumoniae, 1 EBV and 1 adenovirus. All patients were intubated and 6 (75%) used inotropic agents. In outcome, no death occurred, 6 were survived with neurologic sequelae and 2 returned to premorbid normal neurologic status.

Conclusion: Encephalitis was more often the primary cause in RSE. RSE is associated with increased hospital length of stay and functional disability. Morbidity is related to etiology and multifocal or generalized abnormalities on the initial EEG.







CLINICAL STUDY ON STATUS EPILEPTICUS (SE) IN DRAVET SYNDROME (DS)

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Background: SE in DS is therapy-resistant and recurring frequently. We studied the clinical characteristics and better treatment strategy for SE in DS.

Method and Subjects: The subjects were 32 children (M=5, F=27) fulfilling the criteria of DS and undergoing SCN1A mutation analysis. They were followed-up at least for 2 years at our hospital. We retrospectively reviewed the medical record and investigated the clinical features and responses to various treatments for SE.

Results: All patients experienced SE or clusters of the seizures repeatedly on febrile and afebrile states. The age at first SE ranged from 3 months to 3 years and 7 months (mean=9.9 months), and 23 patients experienced the first SE under 1 year of age. SE manifested predomi-

nantly with convulsive SE in 20 cases, clusters of brief seizures in 7 cases and nonconvulsive SE in 5 cases. There were 9 patients repeatedly requiring intravenous pentobarbital anesthesia for the treatment of SE. We administered potassium bromide (BrK) in 25 patients at the mean age of 3 years 11 months, which could successfully control SE in 16 patients (64%). There were no clinical differences in SE between those with and without SCN1A mutations.

Conclusion: SE in DS was often induced by elevated temperature and required intensive treatment at emergency basis during infancy and early childhood. Early introduction of BrK could reduce SE incidence and also might prevent secondary brain dysfunction.

POSTER 20 9th ISS

ELECTRON TRANSPORT CHAIN COMPLEX IV DEFICIENCY PATIENT WITH STATUS EPILEPTICS

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Background: ETC IV deficiency (cytochrome c oxidase deficiency) is associated with various types of mitochondrial encephalomyopathy, and has been recognized as progressive neurologic deterioration, lactic acidemia, and cardiomyopathy. We report a $17^{1/2}$ -year-old girl with COX deficiency who presented with cortical blindness, myoclonic seizures followed by status epilepticus, and progressive white matter change in brain MRI.

Method: Measurement of lactic acid and blood gas, urine organic acid analysis, plasma amino acid analysis, electron transport chain enzyme measurement in skin fibroblast, EEG, and molecular study were carried out. Muscle biopsy and family evaluation were also done.

Case History: A $17^{1/2}$ -year-old girl presented status epilepticus requiring mechanical ventilation after URI symptom. She started myoclonic seizures at 13 years of age with abnormal EEG. At age 14, she had cortical blindness, and seizure frequency increased.

At 15 years of age, she presented with progressive myoclonic seizures, chest pain with exertional dyspnea, abdominal pain, visual problem with progressive cortical blindness, fatigability, hearing impairment, slurred speech, hand tremor and left arm hemiparesis. Her condition has been complicated by weight loss, scalp alopecia, immune suppression presented by pneumonia, herpes zoster, intractable diarrhea. Status epilepticus was controlled by L- carnitine, coenzyme Q, dichlor acetic acid, acyclovir and anticonvulsants.

Results: Biochemical parameter showed blood lactic acid 5.30(N 0.7-2.1), NH₃ 49.1(9-34 mmol/l), plasma alanine 602 (185-537 μ mol/L), and lactate/ pyruvate ratio 33.5(N 8-20). Urine organic acid analysis showed marked elevation of lactic and pyruvic acid. EEG showed sharp waves in the rt. parieto-occipital area and frontocentrotemporal areas. Partial seizure waves from rt. fronto-central region, predominant in lt. hemisphere were observed. Head CT: encephalomalacia in both side occipitoparietal lobe and mild degree diffuse atrophy of the cerebral hemisphere. Brain MRI: both occipital lobe high signal lesion. Mother has migraine, brother has severe lactic acidosis, and displays radiological signs of a leukodystrophic process. The other brother is healthy. Cytochrome $\bar{\mathrm{C}}$ oxidase deficiency (ETC complex IV) 12 (N 57.3-373.0 µmol/ min/g wet weight). We found a novel homoplasmic mutation in the mitochondrial cytochrome c oxidase subunit gene COI. Sequence analysis of mtD-NA resulted in the identification of homoplasmic missense mutation 6417A>G (I171M) in COI.

Conclusions: Mitochondrial disorders should be considered in patients with progressive myoclonic epilepsy, leukodystropy, lactic acidosis and family history of maternal inheritance pattern. Cytochrome C oxidase deficiency could progress to status epilepticus.

ATYPICAL ABSENCE STATUS EPILEPTICUS IN ONE PATIENT WITH CEREBRAL FOLATE DEFICIENCY

POSTER 21 9th ISS

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Background: Cerebral folate deficiency is a newly emerging neurological disease in children. Only a limited number of cases have been diagnosed in the past few years in the world. However, the relationship between cerebral folate deficiency and epilepsy has never been investigated.

Clinical Details: We retrospectively reviewed the seizure and epilepsy patterns in children with cerebral folate deficiency diagnosed in our department. The diagnosis of cerebral folate deficiency was made based on the changes of CSF neurotransmitters and folate levels. Total 70% of the patients suffered from seizure disorders. Of these, a 5-year-old boy presented with psychomotor retardation and involuntary movements. The 24-hr video EEG revealed atypical absence status. After diagnosis to have cerebral folate deficiency, folate was added. The seizures decreased after folic acid supplementation, and antiepileptic drugs (AEDs) can be tapered. **Conclusions:** Seizures are common in children

with cerebral folate deficiency. Treatment with folate will improve the seizure control, and decrease the unnecessary AED use.

A CASE OF CERVICAL MYELITIS AND CEREBRAL VASCULOPATHY CAUSED BY VARICELLA-ZOSTER

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Background: Varicella-zoster viruses (VZV) cause neurological complications in immunosuppressed patients and old people. Here we report an immunocompetent child who developed cervical myelitis and cerebral vasculopathy caused by VZV.

Clinical Details: A 9-year-old boy was admitted due to hyperesthesia and pain in bilateral C2,3,4 dermatome 1 month ago. His father had zoster 6 months ago and he had vesicular eruption with itching and pain on the right post-auricular area five months ago, which were subsided spontaneously. Before admission, he had no admission history and he was healthy. CBC, blood chemistry, IgG, IgM, C3,C4,CH50 were within normal range. CSF findings were clear and negative for WBC and VZV PCR. VZV IgM was equivocal (9.2), IgG was positive (53.2) and CD4/CD8 ratio was inverted (0.9). His brain and C-spine MRI showed chronic encephalomalatic change at the medial frontal gyral area on T2WI, low signal intensity on T1WI. Diffusely increased high signal intensity at the C1-C7 spinal cord without significant enhancement. Stenosis at the right transverse carotid area on MR angiogram. He was medicated acyclovir for 3 weeks and Neurontin for postzoster neuralgia and neuralgia was resolved.

Conclusions: This is a rare case with cerebral mutficocal infarctions due to vasculopathy and cervical myelits, caused by VZV. He has post-zoster neuralgia but no immunologic abnormalities except mild low level of helper T cells. Physician should be aware of these rare complications in the pediatric populations who have no malignancy or immunologic abnormalities.





REFRACTORY STATUS EPILEPTICUS DUE TO HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

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Background: Hemophagocytic lymphohistiocytosis (HLH) caused by hyper activation of T lymphocytes and macrophages is characterized by hypercytokinemia and various symptoms. The involvement of CNS is a rare but fatal complication and the diagnosis at the early stage is difficult. We experienced a case of HLH which is presented as status epilepticus (SE) and describe the clinical details of this case.

Clinical Details: A 7-year-old girl was transferred to another hospital because of convulsion. Since leucocytopenia and thrombocytopenia was detected on laboratory examination, she was refered to our hospital. At the time of admission, consciousness was clear, but she began to have frequent convulsions which evolved to SE. It was not controlled with anticonvulsants (midazolam, phenobarbital, thiamylalsodium). The diagnosis of HLH was confirmed on the result of bone marrow examination and mPSL pulse therapy combined with cyclosporine was started. SE was controlled with this therapy and consciousness recovered. However, SE recurred whenever the therapy was withdrawn.

Conclusions: The suppression of HLH-induced SE with mPSL and immunotherapy suggests that immune system plays an important role in the occurrence of convulsions.

POSTER 24

ACUTE ENCEPHALOPATHY WITH PROLONGED FEBRILE SEIZURE AND LATE REDUCED DIFFUSION (AESD)

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Background: Patients with encephalopathy heralded by a prolonged seizure as the initial symptom often have abnormal subcortical white matter on diffusion weighted magnetic resonance images (DWI). This study was performed to determine whether they share other common features.

Methods: Patients with acute encephalopathy with prolonged febrile seizure and late reduced diffusion (AESD) were collected retrospectively. Their clinical, laboratory, and radiologic data were reviewed.

Results: 17 patients were identified, aged from 10 month to 4 years. All had a prolonged febrile seizure (longer than an hour in 12 patients) as their initial symptom. Subsequent seizures, most often in clusters of complex partial seizures, were seen four to six days after the initial

seizure in 16 patients. Outcome ranged form almost normal to severe mental retardation.

MRI performed within 2 days of presentation showed no abnormality. Subcortical white matter lesions were observed on DWI between 3 and 9 days in all 17 patients. T2-weighted images showed linear high intensity of subcortical Ufibers in 13 patients. The lesions were predominantly frontal or fronto-parietal in location with sparing of the peri-Rolandic region. The diffusion abnormality disappeared between day 9 and 25, and cerebral atrophy was detected later than 2 weeks. Three patients having only frontal lesions had relatively good clinical outcome.

Conclusions: Although the pathophysiologic mechanism remains unknown, these patients seem to have a distinctive encephalopathy syndrome. (*Neurology* in press)

PROLONGED FEBRILE CONVULSION IN CHILDREN

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Background: Prolonged febrile convulsion (PFC) makes up a significant proportion of status epilepticus (SE) in children. The natural history of PFC may be different from that of other SE. This study was conducted to determine the characteristics of PFC in children.

Methods: All patients admitted to Children's Medical Center, Japan Red Cross Nagoya First Hospital between January 1, 2003 and December 31, 2004, were studied retrospectively. Subjects with incidence of SE including PFC were ascertained through the records. We defined SE as a single clinical seizure or series of seizures lasting more than 30 minutes without recovery of consciousness between the seizures. Each episode of SE was reviewed to determine whether it was an acute symptomatic seizure, PFC or epilepsy. We inquired about the clinical characteristics, seizure duration, seizure types, and EEG abnormalities.

Results: There were 59 episodes of SE. 17% had acute symptomatic seizures, 27% had PFC, and 56% had epilepsy. No PFC lasted more than one hour. On the contrary, seizures lasted more than one hour in 80% patients with acute symptomatic seizures and 58% with epilepsy. Focal EEG abnormalities were recorded in acute periods of four PFC patients, and in chronic periods of four.

Conclusion: PFC is a common cause of SE in children. However intractable PFC lasting more than one hour is relatively rare, compared with SE in acute symptomatic seizures or epilepsy.

CONTROVERSIES IN FEBRILE CONVULSION

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Background: Febrile convulsion is one of the commonest neurological problems encountered in paediatric practice. Although it is a benign self limiting syndrome of early childhood, it is a hotly debated subject with controversial issues regarding its definition, classification, diagnostic interventions including lumbar puncture, EEG, blood studies and neuroimaging, prognosis and management.

Summary Points: Febrile convulsion occurs within 24 hours of illness. The temperature threshold varies in the same child and from one child to another. It is classified as simple and complex but debate continues regarding the usage of these terms and their prognostic value. Lumbar puncture in a child with first febrile convulsion should be done as per decision depends on the experience and judgment of physician. EEG is of limited value and not a guide to treatment or prognosis and neuroimaging not recommended. Whether febrile seizures have a causal relationship with mesial temporal sclerosis is also a matter of debate. There are effective therapise to prevent but potential side effects of drugs outweigh their benefit. Intermittent prophylaxis during fever may be effective but long term prognosis is not influenced by that. A practical approach to a child with febrile convulsion is suggested.







ACUTE ENCEPHALITIS WITH REFRACTORY, REPETITIVE PARTIAL SEIZURES : THE PRESENCE OF PROLONGED, PECULIAR INFLAMMATION

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Background: Acute encephalitis with refractory, repetitive partial seizures (AERRPS) is a catastrophic type of para-encephalitic epilepsy, whose etiology is unknown.

Clinical details: We report on three patients with AERRPS, who suffered acute febrile episodes associated with status epilepticus, which necessitated high-dose barbiturate therapy for several weeks. Electroencephalography (EEG) revealed a predominance of diffuse epileptiform discharges initially, subsequently developing into periodic bursts of discharges. Reduction of the barbiturate dosage resulted in clinical and subclinical partial seizures appearing repetitively in clusters. Prolonged fever persisted for 2-3 months, even several weeks after normalization of cell counts in the cerebrospinal fluid. The EEG showed an improvement after resolution of this fever, and seizures became less frequent, although still intractable. Steroid administration was effective in stopping the febrile episodes in one patient, with concurrent improvement in seizure control. Magnetic resonance imaging showed enhancement of bitemporal cortical areas in one patient, and high signal intensity in the bilateral claustrum in another patient. Diffuse cortical atrophy appeared within two months after the onset in all patients.

Conclusions: The evolution of the seizures and EEG findings suggested a high degree of cortical excitability in AERRPS. We hypothesize that a prolonged inflammatory process exists in the cerebral cortex with the etiology described here, and may be pivotal in the epileptogenesis. Consequently, anti-inflammatory therapies may be worth trying during the acute phase of this type of epileptic syndrome.

POSTER **28**

CLINICAL STUDY OF 4 CHILDREN OF ACUTE ENCEPHALITIS WITH REFRACTORY REPETITIVE PARTIAL SEIZURES (AERRPS) WITH HIPPOCAMPAL LESION

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Background: We previously reported "Acute encephalitis with refractory seizures" (1988) which had following features; seizure was secondary generalized which appear within a few days after the onset of postinfectious encephalitis, intractably repeated with intervals less than ten minutes and showed no response to any antiepileptic drugs without intravenous barbiturate anesthesia. Many cases of AERRPS were reported to have hippocampal lesion. Four patients of AERRPS admitted to our hospital and we report these cases with the characteristics of brain MRI.

Clinical Details: Case 1, a 5-year-old male. 10 days of pentobarbital therapy was required. He still had seizure. Case 2 was a 11-year-old female, after HA1-influenza virus infection, pentobarbital for 35 days. She sat after 2 years, had intractable seizure. Case 3 was a 11-year-old male, after HA3-influenza, pentobarbital for 4 days. Case 4 was 4 year-old male. His repetitive seizures required extremely high dose pentobarbital. With decreasing of pentobarbital intractable seizures recurred and he had been under treatment for 11 months since admission. In brain MRI all 4 cases showed hippocampal lesions and 2 cases (case 2 and 4) showed lesions out of limbic system. Except for Case 2, antiglutamate receptor GluR ε 2 antibody was positive. Conclusions: The AERRPS is characterized by extremely high frequency seizures. It seems that frequent seizures lead to hippocampal lesions and that repetitive seizures for long periods also lead to the other lesions such as thalamus and substantia nigra.

A CASE OF ACUTE ENCEPHALITIS WITH REFRACTORY REPETITIVE PARTIAL SEIZURES ACCOMPANIED WITH INVOLVEMENT OF THE BASAL GANGLIA

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Background: Acute encephalitis with refractory repetitive partial seizures (AERRPS) was a catastrophic epilepsy fulfilling the following **criteria:** 1. acute encephalitis with a prolonged acute phase of more than 2 weeks, 2. persistent partial seizures, 3. seizures frequently evolving into convulsive status, 4. extremely intractable, and 5. no causative lesion or agent is identified. We previously reported a patient with AER-RPS who showed choreo-ballistic movements and speculated the basal ganglia involvement. We here report a patient with AERRPS who revealed involuntary movements and showed hyperperfusion of the basal ganglia.

Clinical Details: A 1-year-old healthy girl showed unconsciousness and generalized tonicclonic convulsions on the first febrile day. Cerebrospinal fluid findings were normal. To cease recurrent convulsions, she was treated with midazolam. There were no abnormal findings on CT and MRI on the first and second illness day, respectively. EEG showed rapid rhythms preceding polyspikes on the frontal and central areas. Reccurrent convulsions appeared after termination of midazolam on the 20th illness day. On the 5th illness day, involuntary movements of the head and upper limbs appeared. SPECT on the 13th illness day showed hyperperfusion of the basal ganglia. Clonazepam, valproic acid and potassium bromide succeeded in controlling convulsions and involuntary movements after the 40th illness day.

Conclusions: Involuntary movements originated from the basal ganglia could be clinical symptoms of AERRPS. This observation might be a clue to clarify pathophysiology of AERRPS.

MRI-DIFFUSION WEIGHTED IMAGES OF ENCEPAHLOPATHY ASSOCIATED WITH HUMAN HERPESVIRUS 6

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Department of Pediatrics, Kansai Medical University, Moriguchi and Hirakata, Osaka, Japan

Background: The encephalopathy associated with human herpes virus 6 (HHV-6 encephalopathy) is occasionally seen in Japan. Recently, it was reported that the MRI-diffusion weighted imaging (DWI) is useful not only to diagnose the early stage of HHV-6 encephalopathy, but also the encephalopathy associated with the status epilepticus in children. We report the characteristic findings of DWI in an infant with acute HHV-6 encephalopathy and status epilepticus.

Clinical Details: A 10-months-old previously healthy Japanese girl presented with high fever and left hemi-convulsion on day 1. Her seizure persisted more than 1 hour followed by rapid deterioration of consciousness. The seizure subsided with intravenous diazepam administration. We made the diagnosis of a status of complex partial seizures. On day 4, the exanthema developed on her whole body. On day 5, she had a cluster of short generalized clonic seizures with recrudescence of high fever. Her MRI immediately after these seizures showed high intensity area in the subcortical white matter especially in the right occipital lobe on DWI, while T1- and T2-weighted images were normal. The abnormal findings of affected areas disappeared on day 12 with improvement of clinical symptoms. **Conclusions:** A DWI is useful to diagnose the early phase of HHV-6 encephalopathy and the severity of status epilepticus.



OST



Profiles of Invited Lecturers

Makiko OSAWA

Present Position

Chairman and Professor of the Department of Pediatrics, Tokyo Women's Medical University, School of Medicine (TWMU)

Formal Education

March, 1972: Graduated from Tokyo Women's Medical College (TWMC), (Bachelor of Medicine) March, 1976: Completed post-doctoral dissertation to obtain medical degree (MD), TWMC March, 1978: Obtained Doctor of Medical Science degree (PhD equivalent)

Qualifications

National Board of Medical Examiners of Japan, Certified, June 1972 Passed the ECFMG Examination in the USA, Jan 1973 Certified as a Pediatrician by the Japan Pediatric Society Certified as a Pediatric Neurologist by the Japanese Society of Child Neurology Certified as a Neurologist by the Japan Society of Neurology Certified as a Clinical Geneticist by the Japan Society of Human Genetics

Selected Publications

- Osawa M, ed. The 2004 annual report of the research committee on the clinical evidence of medical treatment for status epileptics in childhood: : Sponsored by the Japanese Ministry of Health, Labour and Welfare, Tokyo, 2005: pp. 194
- 2) **Osawa M**, ed. The 2003 annual report of the research committee on the clinical evidence of medical treatment for status epileptics in childhood: : Sponsored by the Japanese Ministry of Health, Labour and Welfare, Tokyo, 2004: pp133
- 3) **Osawa M**, ed. The 2002 annual report of the research committee on the clinical evidence of medical treatment for status epileptics in childhood: : Sponsored by the Japanese Ministry of Health, Labour and Welfare, Tokyo, 2003: pp105.
- Yanagaki S, Oguni H, Yoshii K, Hayashi K, Imai K, Funatsuka M, Osawa M. Zonisamide for West syndrome: a comparison of clinical responses among different titration rate. Brain Dev 2005; 27: 286-290.
- 5) Ito Y, Gertsen E, Oguni H, Nakayama T, Matsuo M, Funatsuka, Voit T, Klepper J, **Osawa M**. Clinical presentation, EEG studies, and novel mutations in two cases of GLUT1 deficiency syndrome in Japan. Brain Dev 2005; 27: 311-317
- 6) Ohtsu M, Oguni H, Hayashi K, Funasuka M, Imai K, Osawa M. EEG in children with early-onset benign occipital seizure susceptibility syndrome. Panayiotopoulos symdrome Epilepsia 2003: 44 (3): 435-442



Claude G. WASTERLAIN

Education

1961:	MD University of Liege (Belgium)
1964 – 67:	Residency in Neurology at Cornell University Medical College
1969:	L. Sc Free University of Brussels



Positions

1970 – 1975:	Associate Professor of Neurology, Cornell University Medical College,
	New York, NY
1976 - 1979:	Associate Professor of Neurology, University of California School of Medicine,
	Los Angeles, CA
1979 – present:	Professor of Neurology, University of California School of Medicine,
	Los Angeles, CA

Selected Publications

- 1) Wasterlain CG., Mazarati A M, Liu H, Niquet J, Suchomelova L, Naylor D, Langel U, Sankar R. Short-term plasticity of hippocampal neuropeptides and neuronal circuitry in experimental status epilepticus. Epilepsia 2002; 43 (S 5): 20-29.
- 2) Mazarati AM, Bragin A, Baldwin R, Shin D, Wilson C, Sankar R, Naylor D, Engel JJr, **Waster**lain CG. Epileptogenesis after self-sustaining status epilepticus. Epilepsia 2002; 43 (S 5): 74-80.
- 3) Niquet J, Allen SG, Baldwin RA, **Wasterlain CG**. Evidence of caspase-3 activation in hyposmotic stress-induced necrosis. Neurosci Lett. 2004; 356: 225-227.
- 4) Niquet J, Liu H, **Wasterlain CG.** Programmed neuronal necrosis and status epilepticus. Epilepsia 2005; 46 S5: 43-48.
- 5) Naylor DE, **Wasterlain CG**. GABA synapses and the rapid loss of inhibition to dentate gyrus granule cells after brief perforant path stimulation. Epilepsia. 2005; 46, (S5): 142-147.
- 6) Suchomelova L, Baldwin RA, Kubova H, Thompson KW, Sankar R, **Wasterlain CG**. Treatment of experimental status epilepticus in immature rats: dissociation between anticonvulsant and antiepileptogenic effects. Pediatr. Res. 2006; 59(2): 237-243.
Yoko OHTSUKA

Generation 3 Between the second secon

Academic experience

1965 –	71: Medical Studies in Okayama University Medical Scho	ool
1985:	Doctor of Medical Science	
1988:	Lecturer of Child Neurology	
1990:	Specialist in Pediatrics	
1992:	Specialist in Child Neurology	
1995:	Associate Professor of Child Neurology, Okayama Un	iversity
0000		

2003 - present: Professor of Child Neurology, Okayama University Graduate School

Selected publications

- 1) Oka E, **Ohtsuka Y**, Yoshinaga H, Murakami N, Kobayashi K, Ogino T. Prevalence of childhood epilepsy and distribution of epileptic syndromes: a population-based survey in Okayama, Japan. Epilepsia 2006; 47 (in press).
- Ohtsuka Y, Kobayashi K, Yoshinaga H, Ogino T, Ohmori I, Ogawa K, Oka E. Relationship between severity of epilepsy and developmental outcome in Angelman syndrome. Brain Dev 2005; 27: 95-100.
- 3) Kobayashi K, Oka M, Inoue T, Ogino T, Yoshinaga H, **Ohtsuka Y**. Characteristics of slow waves on EEG associayed with epileptic spasms. Epilepsia 2005; 46: 1098-1105.
- 4) Yoshinaga H, **Ohtsuka Y**, Tamai K, Tamura I, Ito M, Ohmori I, Oka E. EEG in childhood absence epilepsy. Seizure 2004; 13: 296-302.
- 5) Ogino T, **Ohtsuka Y**, Ido Y, Mayanagi Y, Watanabe E, Oka E. Memory function decline over 18 months after selective amygdalohippocampectomy. Epileptic Disord 2004; 2: 115-120.
- 6) Ohmori I, **Ohtsuka Y**, Ouchida M, Shimizu K, Oka E. Is phenotype difference in severe myoclonic epilepsy in infancy related to SCN1A mutations? Brain Dev 2003; 25: 488-493.
- 7) **Ohtsuka Y**, Ohmori I, Ogino T, Ouchida M, Shimizu K, Oka E. Paroxysmal movement disorders in severe myoclonic epilepsy in infancy. Brain Dev 2003; 25: 401-405.
- 8) Yoshinaga H, Nakahori T, **Ohtsuka Y**, Oka E, Kitamura Y, Kiriyama H, Kinugasa K, Miyamoto K, Hoshida T. Benefit of simultaneous recording of EEG and EMG in dipole localization. Epilepsia 2002; 43: 924-928.
- 9) **Ohtsuka Y**, Tanaka A, Kobayashi K, Ohta H, Nakano K, Oka E. Childhood-onset epilepsy associated with polymicrogyria. Brain Dev 2002; 24: 758-765.
- 10) Ohmori I, Ouchida M, **Ohtsuka Y**, Oka E, Shimizu K. Significant correlation of the SCN1A mutations and severe myoclonic epilepsy in infancy. BBRC 2002; 295: 17-23.
- 11) **Ohtsuka Y**, Yoshinaga H, Kobayashi K, Murakami N, Yamatogi Y, Oka E, Tsuda T. Predictors and underlying causes of medically intractable localization-related epilepsy in childhood. Pediatr Neurol 2001; 254: 38-42.
- Ohtsuka Y. Refractory childhood epilepsy and factors related to refractoriness. Epilepsia 2000; 41(suppl. 9): 14-17.
- 13) **Ohtsuka Y**, Sato M, Oka E. Nonconvulsive status epilepticus in childhood localization-related epilepsy. Epilepsia 1999; 40: 1003-1010.
- 14) **Ohtsuka Y**, Ohmori I, Oka E. Long-term follow-up of childhood epilepsy associated with tuberous sclerosis. Epilepsia 1998; 39: 1158-1163.

Brian GR NEVILLE

Professor Brian Neville is a UK paediatric neurologist with specific interests in epilepsy and disability. He set up the Guy's Paediatric Neurology Department as the centre for South East Thames and worked there from 1973 to 1989. He moved to the newly created Chair of Paediatric Neurology at the Institute of Child Health (UCL) and Great Ormond Street Hospital for Children where he developed the clinical and academic group as the largest in Europe. In 2004 he



moved to the new Prince of Wales's Chair of Childhood Epilepsy which links the National Centre for Young People with Epilepsy with the above institutions. He has published more than 150 original peer reviewed articles and his current research is particularly related to epileptic encephalopathies.

He has been Secretary and President of the British Paediatric Neurology Association and has worked extensively on UK and European training programmes. He was founder of the European Academy of Childhood Disability.

Selected Original Articles

- 1) Scott RC, Besag FMC, and **Neville BGR**. Buccal midazolam and rectal diazepam for epilepsy [Reply Letter]. Lancet. 22 May 1999; 353: 1796-1798.
- 2) Clark M, Carr L, Reilly S, **Neville BGR**. Worster-Drought syndrome, a mild tetraplegic perisylvian cerebral palsy: A review of 47 cases. Brain 2000; 123: 2160-2170.
- Dale RC, de Souza C, Chong WK, Cox TCS, Harding B, Neville BGR. Acute disseminated encephalomyelitis, multiphasic disseminated encephalomyelitis and multiple sclerosis in children. Brain 2000, 123: 2407-2422.
- Scott RC, Gadian G, King M, W Chong, Cox TC, Neville BGR, Connelly A. Magnetic Resonance Imaging Findings Within 5 Days of Status Epilepticus in Childhood. Brain. 2002 Sep; 125(Pt 9): 1951-9.
- 5) Scott RC, King MD, Gadian DG, **Neville BGR**, Connelly A. Hippocampal abnormalities after prolonged febrile convulsion: a longitudinal MRI study. Brain 2003, 126(11): 2551-2557.
- 6) Devlin AM, Cross JH, Harkness W, Chong WK, Harding B, Vargha-Khadem F, Neville BGR. Clinical outcomes of hemispherectomy for epilepsy in childhood and adolescence. Brain 2003, 126(3): 556-566.
- 7) Sanchez-Carpintero R, **Neville BGR**. Attention ability in children with epilepsy. Epilepsia 2003, 44(10): 1340-1349.
- Neville, BGR, Parascandola R, Farrugia R, Felice A. Sepiapterin reductase deficiency: a congenital dopa-responsive motor and cognitive disorder. Brain 2005; 128: 2291-2296.
- 9) Carter JA, Lees JA, Gona JK, Murira G, Rimba K, Neville BGR, Newton RJC. Severe falciparum malaria and acquired childhood language disorder. Developmental Medicine and Child Neurology 2006: 48: 51-57.

Daisuke TOKUHARA

Education

1998:	M. D. Kansai Medical School
2006:	Ph. D. Pediatrics, Osaka City University Graduate School of
	Medicine

Post-Graduate Training and Present Appointment

- 1998 1999: Resident in Pediatrics, Kansai Medical School
- 1999 2001: Medical staff in Pediatrics, Matsubara City Hospital
- 2001 2002: Medical staff in Pediatrics, Osaka City Sumiyoshi Hospital
- 2006 present: Resident in Pediatrics, Osaka City University Graduate School of Medicine

Publications

- Kawajiri M, Okano Y, Kuno M, Tokuhara D, Hase Y, Inada H, Tashiro F, Miyazaki H, Yamano T. Unregulated Insulin Secretion by Pancreatic Beta Cells in Hyperinsulinism/Hyperammonemia Syndrome: Role of Glutamate Dehydrogenase, ATP-Sensitive Potassium Channel, and Nonselective Cation Channel. Pediatr Res. 2006; 59: 359-364.
- 2) **Tokuhara D**, Yokoi T, Nakajima R, Hattori H, Matsuoka O, Yamano T. Time course changes of estrogen receptor alpha expression in the adult rat hippocampus after kainic acid-induced status epilepticus. Acta Neuropathol. 2005; 110: 411-416.
- 3) Tamamori A, Fujimoto A, Okano Y, Kobayashi K, Saheki T, Tagami Y, Takei H, Shigematsu Y, Hata I, Ozaki H, **Tokuhara D**, Nishimura Y, Yorifuji T, Igarashi N, Ohura T, Shimizu T, Inui K, Sakai N, Abukawa D, Miyakawa T, Matsumori M, Ban K, Kaneko H, Yamano T. Effects of citrin deficiency in the perinatal period: feasibility of newborn mass screening for citrin deficiency. Pediatr Res. 2004; 56: 608-614.
- 4) Takaya J, Muneyuki M, **Tokuhara D**, Takada K, Hamada Y, Kobayashi Y. Congenital dilatation of the bile duct: changes in diagnostic tools over the past 19 years. Pediatr Int. 2003; 45: 383-387.



9th ISS

Yoshiya L. MURASHIMA

Educational Qualifications

1981:	M. D. Faculty of Medicine, University of Tokyo
\square 1984:	Ph. D. Neurochemistry Postgraduate school of Tokyo University

Academic Carriers

1984 – 1992:	Section Chief, Department of Neurophysiology, Tokyo Institute of Psychiatry
1992 – 2001:	Department Director, Department of Neurophysiology, Tokyo Institute of Psychiatry
2001 – 2004:	Department Director, Department of Neuroal plasticityy, Tokyo Institute
	of Psychiatry
2004 - present:	Principal Research Scientist, Division of Psychobiology, Tokyo Institute
	of Psychiatry

Publications

- 1) **Murashima YL,** Suzuki J, Yoshii M. Developmental program of epileptogenesis in the Brain of EL mice. Epilepsia 2005; 46 (suppl 5): 10-16.
- 2) **Murashima YL,** Suzuki J, Yoshii M. Molecular mechanism of DNA fragmentation without cell loss in the mutant EL mice brain 82-84 Neurology Asia 2005; 9 (suppl 1): 82-83.
- Murashima YL, Suzuki J, Yoshii M. Ictogenesis and epilepotogenesis in epileptic mutant ELmice. Focus on epilepsy research. Ed. Benjamin SM Nova Science publisher Co. Ltd. NY 2005, 139-198.
- Murashima YL, Yoshii M, Suzuki J. Ictogenesis and epileptogenesis in EL mice Epilepsia. 2003; 43: 130-135.
- 5) **Murashima YL,** Yoshii M, Suzuki J. Role of Nitric oxide synthetase (NOS) in the epileptogenesis in EL mice. Epilepsia 2002; 41 : 195-199.

Raman SANKER

Education

1986:	MD Tulane Medical School. New Orleans, Louisiana	
1986 - 1988:	Pediatric Intern-Resident at Children's Hospital, Los Angeles,	
	California	1
1988 - 1989:	Resident, department of Neurology, UCLA School of Medicine,	
	Los Angeles, Calfornia	
1989 – 1991:	fellow, Division of Pediatric Neurology, UCLA School of Medicine, Los An	ngeles,
	Calfornia	

Present Position

2005 – Present: Professor and Chief, Rubin Brown Chair, Division of Pediatric neurology, David Gaffen School of Medicine at UCLA, California

Selected Publications

- Sankar R, Thamotharan S, Shin D, Moley KH, Devaskar SU. Insulin-responsive glucose transporters-GLUT8 and GLUT4 are expressed in the developing mammalian brain. Brain Res Mol Brain Res. 2002 Nov 15; 107(2): 157-65.
- Sankar R. Can the Long-Term Outcome After Status Epilepticus Be Modified? Epilepsy Curr. 2002 Jul; 2(4): 129-130.
- 3) Sankar R, Wheless JW, Dravet C, Guerrini R, Medina MT, Bureau M, Genton P, Delgado-Escueta AV. Treatment of myoclonic epilepsies in infancy and early childhood. Adv Neurol. 2005; 95: 289-98.
- Caplan R, Sagun J, Siddarth P, Gurbani S, Koh S, Gowrinathan R, Sankar R. Social competence in pediatric epilepsy: insights into underlying mechanisms. Epilepsy Behav. 2005 6(2): 218-28.
- 5) Suchomelova L, Baldwin RA, Kubova H, Thompson KW, **Sankar R**, Wasterlain CG. Treatment of experimental status epilepticus in immature rats: dissociation between anticonvulsant and antiepileptogenic effects.

Pediatr Res. 2006: 59(2): 237-43.

Brian GR NEVILLE

Please refer to 4



9th ISS

Takuya TANABE

Education

1989:	Graduate from Osaka Medical College
$^{-1}$ 1995:	M. D. Graduate from a postgraduate school, Osaka Medical
	College



Post-Graduate Training and Present Appointment

1989:	Resident of department of pediatrics, Osaka Medical College
1995:	Doctor of the division of Pediatrics, Hirakata City Hospital
2002:	Sub director of division of pediatrics, Hirakata City Hospital
2004 - present:	Chief director of division of pediatrics, Hirakata City Hospital
	Assistant professor of clinical education, Osaka Medical College

Selected publications

- 1) Tanabe T. et al. Prospective study of first unprovoked seizure. No to Hattatsu 2005; 37: 461-6.
- 2) **Tanabe T**. et al. Survey of vaccination and viral infections for children with severe myoclonic epilepsy in infancy. *No to Hattatsu* 2004; 36: 318-23.
- 3) Kashiwagi M, **Tanabe T**. et al. Differential diagnosis in children having delirium associated with high fever. *No to Hattatsu* 2003; 35: 310-5.
- 4) **Tanabe T**. et al. Familial epilepsy with hippocampal abnormality in elderly sister. Osaka J Epilepsy Res. 2003; 14: 37-42.
- 5) Takitani K, Nishino A, **Tanabe T**. et al. White matter lesion due to dural sinus thrombosis in an infant with subdural hematoma. *Pediatrics Int*. 2002; 44: 680-2.
- 6) **Tanabe T**. et al. Cerebrospinal fluid and serum neuron-specific enolase levels after febrile seizures. *Epilepsia* 42: 504-507, 2001
- 7) Shichiri M, **Tanabe T**. et al. Usefulness of Near-infrared Spectroscopy for identification of epileptic foci in two localization-related epilepsy patients. *No To Hattatsu* 2001; 33: 475-9.
- 8) **Tanabe T**. et al. Intravenous lidocaine treatment in prolonged or clustering seizures in childhood. *Epilepsia* 2001; 42 (Suppl): 55-6.
- 9) **Tanabe T**. et al. Problems of intravenous lidocaine treatment in status epilepticus or clustering seizures in childhood. *No To Hattatsu* 1999; 31: 14-20.
- 10) Tanabe T. et al. Evaluation of seizure types and photosensitive responses in patients who suffered epileptic seizures while watching an animated TV program called Pocket Monsters. J Jpn Pediatr Soc. 1999; 103: 19-23.

9th ISS

Jun NATSUME

Position

Assistant Professor, Department of Pediatrics, Nagoya University Graduate School of Medicine, Nagoya

Education

1990:	M. D., Nagoya University School of Medicine, Nagoya
1998:	Ph. D., Nagoya University Graduate School of Medicine, Nagoya

Occupation

1990 – 1993: Residency, Department of Pediatrics, Anjo Kosei Hospital
1993 – 1994: Department of Pediatrics, Nagoya University Hospital
1998 – 1999: Department of Pediatrics, Gifu Social Insurance Hospital
1999 – 2002: Post-Doctoral Fellowship, Department of Neurology and Neurosurgery, Montreal Neurological Institute and Hospital, Montreal, Canada
2002 – 2005: Department of Pediatrics, Japanese Red Cross Nagoya First Hospital
2005 – 2006: Department of Pediatrics, Nagoya University Hospital

Selected Publications

- Natsume J, Bernasconi A, Diksic M. Neocortical Epilepsy: α-methyl-L-tryptophan and positron emission tomography studies. 123-130. In Bioimaging in neurodegeneration. Broderick PA, Rahni DN, Kolodny EH. Ed. Humana Press. 2005
- 2) Bernasconi N, **Natsume J**, Bernasconi A. Progression in temporal lobe epilepsy: differential atrophy in mesial temporal structures. Neurology 2005; 65(2): 223-8.
- 3) **Natsume J**, Bernasconi N, Andermann F, Bernasconi A. MRI volumetry of the thalamus in temporal, extratemporal and idiopathic generalized epilepsy. Neurology 2003; 60(8): 1296-1300.
- 4) **Natsume J**, Kumakura Y, Bernasconi N, Soucy J-P, Nakai A, Rosa P, Fedi M. Dubeau F, Andermann F, Lisbona R, Bernasconi A, and Diksic M. α -[¹¹C] methyl-L-tryptophan and glucose metabolism in patients with temporal lobe epilepsy. Neurology 2003; 60(5): 756-761.
- 5) Bernasconi A., Bernasconi N., **Natsume J.**, Antel S. B., Andermann F., Arnold D. L. Magnetic resonance spectroscopy and imaging of the thalamus in idiopathic generalized epilepsy. Brain 2003; 126(11): 2447-54.



Kenji SUGAI

Position

9th ISS

Physician-in-Chief, Department of Child Neurology, NCNP, Japan

Education



1977:	B. Health Sci.	The University of Tokyo School of Health Sciences
1981:	M. D.	The University of Tokyo School of Medicine
1994:	Ph. D.	Toho University School of Medicine

Postgraduate Training and Professional Experience:

1981 – 1983:	Resident, Department of Pediatrics, Kanagawa Children's Medical Center,
	Yokohama, Japan
1983 – 1985:	Resident, Department of Child Neurology, National Center of Neurology and
	Psychiatry (NCNP), Tokyo, Japan
1986 – 1989:	Instructor, Department of Child Neurology, NCNP, Tokyo, Japan
1989 – 1992:	Director, Department of Pediatrics, Nishi-Kohfu National Hospital, Kohfu, Japan
1992 – 1993:	Section chief, Department of Child Neurology, NCNP, Tokyo, Japan
1993 – 1994:	Research fellow, Department of Neurology, Boston Children's Hospital, Harvard
	University, Boston, MA, USA
1994 – 2004:	Section chief, Department of Child Neurology, NCNP, Tokyo, Japan
2004 - present:	Physician-in-Chief, Department of Child Neurology, NCNP, Tokyo, Japan

Selected publications

- 1) Nobutoki T, **Sugai K**, Fukumizu M, Hanaoka S, Sasaki M. Continuous midazolam infusion for refractory nonconvulsive status epilepticus in children. No To Hattatsu 2005; 37(5): 369-73.
- 2) **Sugai K**. Clobazam as a new antiepileptic drug and clorazepate dipotassium as an alternative antiepileptic drug in Japan. Epilepsia 2004; 45 Suppl 8: 20-5.
- 3) Sudoh A, **Sugai K**, Miyamoto T, Mimaki M, Fukumizu M, Hanaoka S, Sasaki M. Non-intravenous high-dose phenobarbital therapy for status epilepticus refractory to continuous infusion of midazolam or pentobarbital: report of three cases. No To Hattatsu 2002; 34(1): 23-9.
- 4) Ozawa H, Kawada Y, Noma S, **Sugai K**. Oral high-dose phenobarbital therapy for early infantile epileptic encephalopathy. Pediatr Neurol 2002; 26: 222-4.
- 5) **Sugai K**, Fukuyama Y, Yasuda K, Fujimoto S, Ohtsu M, Ohta H, Ogawa A, Hamano, S, Hirano S, Yoshioka H, Ishikawa A, Seki T, Itokazu N, Tawa R. Clinical and pedigree study on familial cases of West syndrome in Japan. Brain Dev 2001; 23: 558-64.
- 6) **Sugai K**. Pentobarbital therapy for status epilepticus. Jap J Developmenatl Pharmacology and Therapeutics 1997; 10: 49-52.
- 7) Kinoshita H, Nakagawa E, Iwasaki Y, Hanaoka S, **Sugai K**. Pentobarbital therapy for status epilepticus in children: timing of tapering. Pediatr Neurol 1995; 13: 164-8.
- 8) **Sugai K**. Seizures with clonazepam: discontinuation and suggestions for safe discontinuation rates in children. Epilepsia 1993; 34: 1089-97.
- 9) **Sugai K**, Sakuragawa N, Arima M. Intravenous administration of anticonvulsants under EEG monitoring in ESES: rapid prediction of the efficacy of oral administration of drugs. Jpn J Psychiatry Neurol 1992; 46: 452-4.

Kitami HAYASHI

Date of Birth January 9th 1954

Education

1973 - 1979: Chiba University, School of Medicine, Chiba, Japan



Work History

- 1979 1984: Department of Pediatrics, Japanese Red Cross Medical Center, Tokyo
- 1984 2006: Department of Pediatrics, Tokyo Women's Medical University, Tokyo Appointments
- 1995 –: Assistant Professor, Department of Pediatrics, Tokyo Women's Medical University
- 2006 -: Associate Professor, Department of Pediatrics, Tokyo Women's Medical University

List of Publication

- 1) Hayashi K, Suzuki N, Miyamoto A, et al. A Clinical Study of Deceased Cases of Severe Myoclonic Epilepsy in Infancy. J Jap Epil Soc 1993; 11: 205-210 (in Japanese)
- 2) Hayashi K, Oguni H, Osawa M, et al. Clinical Study of Childhood Epilepsies with Onset in the First Year of Life: A New International Classification of Epilepsies and Epileptic Syndrome. J Tokyo Wom Med Colle 1995; 65(9): 758-767 (in Japanese)
- 3) Hayashi K, Oguni H, Osawa M et al. Clinical Study of Childhood Epilepsies with Onset in the First Year of Life : Clinical Features of Epilepsies with Fever Sensitive Seizures. J Tokyo Wom Med Colle 1995; 65(9): 768-777 (in Japanese)
- 4) **Hayashi K**, Sakauchi M, Oguni H, et al. Clinical Usefulness of Lidocaine in Managing Cluster of Convulsion. Jap J Dev Pharmacol Ther 1997; 10: 102-104 (in Japanese)
- 5) **Hayashi K**, Sakauchi M, Oguni H and Osawa M. Efficacy of continuous intravenous lidocaine in the management of clusters of seizures. J Tokyo Wom Med Univ 2000; 70(EXT): E32-E39.

Veena KALRA

Education

Delhi University (India) MBBS (1968); AIIMS (New Delhi) MD (1972).

Present Position

Professor & Head of Pediatrics, All India Institute of Medical Sciences (AIIMS), Ansari Nagar, New Delhi, India

Publications

Over 120 original research publications in areas of child neurology, hepatic and neuro-genetic disorders of children. Guided 27 MD/Ph. D theses. Authored 20 chapters for Indian and Foreign medical text books. Also authored a book on 'Practical Pediatric Neurology' in 2002.

- 1) Gulati S, Saxena A, Kumar V, **Kalra V**. Duchenne muscular dystrophy: prevalence and patterns of cardiac involvement. Indian J Pediatr. 2005; 72(5): 389-93.
- 2) Kalra V, Seth R, Sapra S. Autism -- experiences in a tertiary care hospital. Indian J Pediatr. 2005; 72(3): 227-30.
- 3) Gulati S, **Kalra V**, Sridhar MR. Status epilepticus in Indian children in a tertiary care center. Indian J Pediatr. 2005; 72(2): 105-8
- Garg A, Gulati S, Gupta V, Kalra V. Congenital muscular dystrophy with characteristic radiological findings similar to those with Fukuyama congenital muscular dystrophy. Neurol India. 2004; 52(4): 496-8.
- 5) Gulati S, Salhotra A, Sharma MC, Sarkar C, **Kalra V**. Central core disease. Indian J Pediatr. 2004; 71(11): 1021-4.
- 6) Gulati S, Menon S, Kabra M, **Kalra V**. Intermittent hyperammonemic encephalopathy in a child with ornithine transcarbamylase deficiency. Indian J Pediatr. 2004; 71(7): 645-7.
- 7) Gulati S, Kalra V. Stroke in children. Indian J Pediatr. 2003; 70(8): 639-48.
- 8) Gulati S, Shah T, Menon S, Jayasundar R, **Kalra V**. Magnetic resonance spectroscopy in pediatric neurology. Indian J Pediatr. 2003; 70(4): 317-25.
- 9) Kalra V. Management of childhood epilepsy. Indian J Pediatr. 2003 Feb; 70(2): 147-51.
- 10) Gulati S, Gera S, Menon PS, Kabra M, **Kalra V**. Hypothalamic hamartoma, gelastic epilepsy, precocious puberty--a diffuse cerebral dysgenesis. Brain Dev. 2002; 24(8): 784-6
- 11) Kalra V, Gulati S, Pandey RM, Menon S. West syndrome and other infantile epileptic encephalopathies--Indian hospital experience. Brain Dev. 2002; 24(2): 130-9





Hideji HATTORI

Education and Present Position

1080.	M. D. Osaka City University School of Medicine
1900.	M. D., Osaka City University School of Medicine
1989:	Ph. D., Osaka City University School of Medicine
	Post-Graduate Training and Present Appointment
1992 – 1998:	Assistant Professor, Department of Pediatrics, Osaka City
	University School of Medicine
1998 – 2000:	Lecturer, Department of Pediatrics, Osaka City University School of
2000 – present:	Lecturer, Department of Pediatrics, Osaka City University Graduate

2000 – present: Lecturer, Department of Pediatrics, Osaka City University G Medicine

Selected Publications

- 1) Tokuhara D, Yokoi T, Nakajima R, **Hattori H**, Matsuoka O, and Yamano T. Time course changes of estrogen receptor alpha expression in the adult rat hippocampus after kainic acid-induced status epilepticus. Acta Neuropathol (Berl). 110: 411-416, 2005.
- Hattori H, Yamano T, Hayashi K, Osawa M, Hamano S, and Kaneko K. Efficacy of Intravenous Lidocaine Therapy in the Management of Status Epileptics in Childhood. Epilepsia 46(Suppl. 2); 4, 2005
- 3) Hattori H, Ohnishi S, Nakagawa Y, Ikemiya M, Yamato K, Matsuoka O, Yokoyama T, and Yamano T. An infant with idiopathic orbital myositis poorly responsive to steroid therapy: a case report. Brain Dev 27; 160-162,2005
- 4) Sakamoto S, Tsuyuguchi N, Takami T, Morino M, Goto T, **Hattori H**, Tsutada T, Haque M, Sunada I, Shimogawara M, and Hara M. Interictal Patterns of Cerebral Glucose Metabolism, Perfusion, and Magnetic Field in Mesial Temporal Lobe Epilepsy. Epilepsia. 44: 1196-1206, 2003.
- 5) **Hattori H**, Mastuoka O, Ishida H, Hisatsune S, and Yamano T. Magnetic Resonance Imaging in Occipital Lobe Epilepsy with Frequent Seizures. Pediatric Neurology 28(3); 216-218, 2003
- 6) Tsutada T, Ikeda H, Tsuyuguchi N, **Hattori H**, Shimogawara M, Shimada H, Miki T. Detecting functional asymmetries through the dipole moment of magnetoencephaloghraphy. J Neurological Sciences 198; 51-61,2002
- 7) Goto T, Tsuyuguchi N, Ohata K, Tsutada T, **Hattori H**, Shimogawara M, Matusaka Y, Sakamoto S, and Hara M. Usefulness of somatosensory evoked magnetic field dipole measurements by magnetoencephalogrphy for assessing spinal cord function. J Neurosurg (Spine 1) 96: 62-67,2002
- 8) **Hattori H**, Yamano T, Kawawaki H, Tsutada T, Tsuyuguchi N, and Shimogawara M. MEG in the detection of focal lesions of West syndrome. Brain Dev 23; 528-32, 2001
- 9) Seto T, Kono K, Kyoko M, Inoue Y, Shintaku H, **Hattori H**, Matsuoka O, Yamano T, and Tanaka A. Brain magnetic resonance imaging in 23 patients with mucopolysaccharaidoses and the effect of bone marrow transplantation. Ann Neurol 2001; 50: 79-92
- 10) Yasunari T, Shiraki K, **Hattori H**, Miki T. Frequency of choroidal abnormalities in neurofibromatosis type I. Lancet 356; 988-92,2000



Medicine School of

Selina Husna BANU

9th ISS

Dr. Selina Husna Banu, MBBS, DCH(DU), PhD(London) Pediatric neurophysiologist & epileptologist Child Development and Neurology Unit, Dhaka Shishu (Children's) Hospital Bangladesh Institute of Child Health, Sher-e-Banglanagar Dhaka-1207; Bangladesh e-address: selina_h_banu@yahoo. com



Clinical and Academic Experiences:

Completed M. B. B. S. from University of Chittagong in 1985, after the internship training, posted at the thana health complex under the Ministry of Health, Bangladesh. Post-graduate training in paediatric medicine for one year in 1989 from Dhaka Shishu Hospital (BICH). Obtained DCH degree at BICH under the University of Dhaka in 1992. Completed PhD in childhood epilepsy at the Neuroscience Unit, University College London in 2003. In 1992 joined the Child Development and Neurology Unit and started career in the field of child neurology and neurodisability. In 1995 got an intense training in clinical neurophysiology and childhood epilepsy in Great- Ormond Street Hospital for Children, Institute of Child Health (ICH), London for one year. In 1996, established the EEG service for children for the first time in the country in collaboration with a private clinic in the city. Later I established the neurophysiology laboratory in Bangladesh Institute of Child Health with the help of ICH London. Trained up technicians, physicians in digital equipment handling, appropriate EEG recording from very young to older children, analysis and clinical correlation of the EEG findings. Has experience in teaching and training the postgraduate students. Organized workshop and seminars in childhood epilepsy to train up physicians in the country. Acted as technical coordinator to establish multidisciplinary service in other district hospitals in the country. Attended international seminars on childhood epilepsy, presented research papers at the national and international seminars and meetings.

Personal Status:

I am married, my husband is a pharmacist, doing a responsible job as an executive director, operation at the national pharmaceutical company. I have two daughters. My hobbies are reading, singing, traveling and knowing people.

Hiroshi OTSUBO

Qualifications

Qualification		6
1983:	Graduate Shinshu University, School of Medicine	th ISS
	Department of Neurosurgery, Shinshu University, School of	
	Medicine	
1988:	Research fellow, Division of Neurosurgery, The Hospital for Sick	
	Children	
1989 – 1990:	EEG Fellow, EEG & Clinical Neurophysiology, Laboratory, The Hospital for Sick	
	Children	
1994 – 1997:	Technical Director, Division of Neurology, The Hospital for Sick Children	
1994 – present:	Assistant Professor, Department of Pediatrics and Medicine, University of Toronto,	
	The Hospital forSick Children	
1997 – present:	Director of Operations EEG & Clinical Neurophysiology and Epilepsy Monitoring	
	Unit (EMU)	

Present Position

Director of Operations, Clinical Neurophysiology & Epilepsy Monitoring Unit, Division of Neurology Project Director, Research Institute, The Hospital for Sick Children Assistant Professor, Department of Pediatrics, The Hospital for Sick Children Associate Scientist, Department of Pediatrics, The Hospital for Sick Children Visiting professor, Shinshu University, School of Medicine

Publications:

- 1) Iida K, Otsubo H, Matsumoto Y, Ochi A, Oishi M, Holowka S, Pang E, Elliott I, Weiss SK, Chuang SH, OC Snead III, Rutka JT. Characterizing magnetic spike sources by using magnetoencephalography-guided neuronavigation in epilepsy surgery in pediatric patients. Journal of Neurosurgery (Pediatrics 2) 2005; 102: 187-196.
- 2) Otsubo H, Iida K, Okuda C, Ochi A, Pang E, Weiss SK, Chuang S, Rutka JT, Snead OC III. Neurophysiological findings of Neuronal Migration Disorders: Intrinsic epileptogenicity of focal cortical dysplasia on EEG, ECoG, and MEG. Journal of Child Neurology. 2005; 20: 357-363.
- 3) Iida K, Otsubo H, Mohamed I, Okuda C, Ochi A, Weiss SK, Chuang SH, Snead OC III. Characterizing magnetoencephalographic spike sources in children with tuberous sclerosis complex. Epilepsia 2005; 46: 1510-1517.
- 4) Ochi A, Otsubo H, Iida K, Elliott I, Weiss SK, Kutomi T, Nakayam T, Sharma R, Chuang SH, Rutka JT, OC Snead III. A comparison of the predominant lateralization of EEG and MEG dipoles in children with intractable epilepsy. Journal of Child Neurology 2005; 20: 885-892.
- 5) Xiao Z, Xiang J, Holowka S, Hunjan A, Sharma R, Otsubo H, Chuang S. Volumetric localization of epileptic activities in tuberous sclerosis using systhetic aperture magnetometry. Pediatr Radiol 2006; 36: 16-21.
- 6) Oishi M, Kameyama S, Masuda H, Tohyama J, Kanazawa O, Sasagawa M, Otsubo H. Single and multiple clusters of magnetoencephalographic dipoles in neocortical epilepsy: Significance in characterizing the epileptogenic zone. Epilepsia 2006; 47: 355-364.

Andrew L. LUX

Qualifications

- 1998: Diploma of the London School of Hygiene & Tropical Medicine from London University.
- 1997: Master of Science in Medical Statistics from University of London
- 1996: Fellow of the Royal College of Pediatrics and Childhealth
- 1993: Member o the Royal College of Physicians
- 1987: Bachelor of Medical Science from University of Nothingham Medical School, Nothingham

Present Position

Locum Consultant in Pediatric Neurology, United Bristol Healthcare NHS Trust and Honorary Locum Consultant with North Bristol NHS Trust

Selected Publications

- Lux AL, Edwards SW, Hancock E, Johnson AL, Kennedy CR, Newton RW, O'Callaghan FJ, Verity CM, Osborne JP; United Kingdom Infantile Spasms Study. The United Kingdom Infantile Spasms Study (UKISS) comparing hormone treatment with vigabatrin on developmental and epilepsy outcomes to age 14 months: a multicentre randomised trial. Lancet Neurol. 2005; 4(11): 712-7.
- 2) Lux AL, Edwards SW, Hancock E, Johnson AL, Kennedy CR, Newton RW, O'Callaghan FJ, Verity CM, Osborne JP. The United Kingdom Infantile Spasms Study comparing vigabatrin with prednisolone or tetracosactide at 14 days: a multicentre, randomised controlled trial. Lancet. 2004 13-19; 364(9447): 1773-8.
- Lux AL, Osborne JP. A proposal for case definitions and outcome measures in studies of infantile spasms and West syndrome: consensus statement of the West Delphi group. Epilepsia. 2004; 45(11): 1416-28.
- 4) Lux AL. West & son: the origins of West syndrome. Brain Dev. 2001 ; 23(7): 443-6.
- 5) Lux AL, Henderson AJ, Pocock SJ. Wheeze associated with prenatal tobacco smoke exposure: a prospective, longitudinal study. ALSPAC Study Team. Arch Dis Child. 2000 Oct; 83(4): 307-12.



Takahito INOUE

Position

1999 – present: Assistant professor, Department of Pediatrics, Fukuoka University School of Medicine

Education

1992:	M. D. Fukuoka University School of Medicine
1999:	Ph. D., Molecular Biology, Kyushu University School of Medicine

Main Publications

- 1) Tsurusawa R, Ohfu M, Masuzaki M, **Inoue T**, Yasumoto S, Mitsudome A. A case of parietal lobe epilepsy with ictal laughter, *No To Hattatsu*. 2005 Jan; 37(1): 60-4. Japanese.
- 2) Fukuma G, Oguni H, Shirasaka Y, Watanabe K, Miyajima T, Yasumoto S, Ohfu M, Inoue T, Watanachai A, Kira R, Matsuo M, Muranaka H, Sofue F, Zhang B, Kaneko S, Mitsudome A, Hirose S. Mutations of neuronal voltage-gated Na+ channel α1 subunit gene SCN1A in core severe myoclonic epilepsy in infancy (SMEI) and borderline SMEI (SMEB), *Epilepsia* 2004 Feb; 45(2): 140-8.
- 3) Ohfu M, Masuzaki M, Inoue S, **Inoue T**, Yasumoto S, Ogawa A, Tomoda Y, Tsuru N, Mitsudome A. Interleukin-6 in the cerebrospinal fluid of two patients with herpes zoster meningitis, *No To Hat*-*tatsu*. 2001 May; 33(3): 270-5. Japanese.
- Hirose S, Zenri F, Akiyoshi H, Fukuma G, Iwata H, Inoue T, Yonetani M, Tsutsumi M, Muranaka H, Kurokawa T, Hanai T, Wada K, Kaneko S, Mitsudome A. A novel mutation of KCNQ3 (c. 925T-->C) in a Japanese family with benign familial neonatal convulsions, *Ann Neurol.* 2000 Jun; 47(6): 822-6.
- 5) **Inoue T**, Yamaza H, Sakai Y, Mizuno S, Ohno M, Hamasaki N, Fukumaki Y. Position-independent human beta-globin gene expression mediated by a recombinant adeno-associated virus vector carrying the chicken beta-globin insulator. *J Hum Genet*. 1999; 44(3): 152-62.
- 6) Furuumi H, Firdous N, **Inoue T**, Ohta H, Winichagoon P, Fucharoen S, Fukumaki Y. Molecular basis of beta-thalassemia in the Maldives, *Hemoglobin*. 1998 Mar; 22(2): 141-51.

Claude G. WASTERLAIN

Please refer to 2





Masashi MIZUGUCHI

Position

9th ISS

Associate Professor, Department of Pediatrics, Graduate School of Medicine, the University of Tokyo

Education

1980:	M. D., University of Tokyo, Faculty of Medicine
1989:	Ph. D., University of Tokyo, Faculty of Medicine

Occupation

1980 – 1983:	Pediatrics Residency, Tokyo University Hospital and Tokyo Metropolitan Fuchu		
	Hospital		
1983 – 1986:	Pediatric Neurology Residency, Tokyo Metropolitan Neurological Hospital		
1986 – 1988:	Pathology Residency, Tokyo University Hospital,		
1988 – 1989:	Assistant, Department of Neuropathology, Brain Research Institute, University		
	Tokyo		
1989 – 1991:	Postdoctoral fellow, Department of Medicine, University of British Columbia		
1991 – 1993:	Assistant, Department of Pediatrics, University of Tokyo		
1993 – 1995:	Section Chief, Department of Mental Retardation and Birth Defect Research, Na-		
	tional Institute of Neuroscience		
1996 – 2004:	Associate Professor, Department of Pediatrics, Jichi Medical School,		
1996 – present:	Associate Professor, Department of Pediatrics, University of Tokyo		

Main Publication List

- Yamanouchi H, Kawaguchi N, Mori M, Imataka G, Yamagata T, Hashimoto T, Momoi M, Eguchi M, Mizuguchi M. Acute infantile encephalopathy predominantly affecting the frontal lobes. Pediatr Neurol 2006; 34: 93-100.
- 2) Mastroyianni, SD, Gionnis D, Voudris K, Skardoutsou A, **Mizuguchi M**. Acute necrotizing encephalopathy of childhood in non-Asian patients. Report of 3 cases and literature review. J Child Neurol 2006; in press.
- 3) Nakai Y, Itoh M, Mizuguchi M, Ozawa H, Okazaki E, Kobayashi Y, Takahashi M, Ohtani K, Ogawa A, Narita M, Togashi T, Takashima S. Apoptosis and microglial activation in influenza encephalopathy. Acta Neuropathol 2003; 105: 233-239. Mizuguchi M, Hayashi M, Nakano I, Kuwashima M, Yoshida K, Nakai Y, Itoh M, Takashima S. Concentric structure of thalamic lesions of acute necrotizing encephalopathy. Neuroradiology 2002; 44: 489-493.
- 4) **Mizuguchi M**. Acute necrotizing encephalopathy of childhood: a novel form of acute encephalopathy prevalent in Japan and Taiwan. Brain Dev 1997; 19: 81-92.
- 5) **Mizuguchi M**, Abe J, Mikkaichi K, Noma S, Yoshida K, Yamanaka T, Kamoshita S. Acute necrotising encephalopathy of childhood: a new syndrome presenting with multifocal, symmetric brain lesions. J Neurol Neurosurg Psychiatry 1995; 58: 555-561.



Masashi SHIOMI

Education:

1976:	MD. Osaka University School of Medicine		
1990:	Ph. D., Medicine, Osaka University School of Medicine		



Professional Training and Employment

1976 – 1977:	Resident in Pediatrics. Osaka University Hospital
1977 – 1978:	Medical Staff in Pediatrics, Ashiya Municipal Hospital
1978 – 1979:	Medical Staff in Neonatology, Aizenhashi Hospital
1980 – 1994:	Medical Staff in Pediatrics and Infectious Disease, Momoyama Hospital
1994 – 1996:	Medical Staff in Pediatrics and Infectious Disease, Osaka City General Hospital
1997 – present:	Chief in Pediatric Emergency Medicine and Infectious Disease

Selected Publications:

- 1) **Shiomi M**. Therapeutic level of theophylline is the possible cause of acute encephalopathy with febrile convulsive status epilepticus (AEFCSE). Japanese J Pediatrics 2006; 59: 187-96 (in Japanese)
- 2) Kaida A, **Shiomi M**, et al. Seasonal distribution and phylogenetic analysis of human metapneumovirus among children in Osaka City, Japan J Clin Virol 2006; 35: in press
- 3) **Shiomi M**. the clinical spectrum of influenza encephalopathy. Japanese J Pediatric Medicine 2003; 35: 1676-81 (in Japanese)
- 4) Shiomi M. Influenza Encephalopathy. Nippon Rinsho. 2003; 61: Suppl 2, 100-6
- 5) Tano Y, **Shiomi M**, et al. Rapid serological diagnosis of enterovirus 71 infection by IgM ELISA. Jpn J Infect Dis. 2002; 55: 133-5
- 6) Komiyama M, **Shiomi M**, et al. An additional variant of the persistent primitive trigeminal artery: accessory meningeal artery--antero-superior cerebellar artery anastomosis associated with moyamoya disease. Acta Neurochir (Wien). 1998; 140: 1037-42
- 7) **Shiomi M**, et al. Effect of early oral fluoroquinolones in hemorrhagic colitis due to Escherichia coli O157: H7 Pediatr Int. 1999; 41: 228-232

Yoshihiro MAEGAKI

Education

1988:

9th ISS

M. D. Tottori University Faculty of Medicine



Post-Graduate Training and Present Appointment

1000 1000.	Dedictuics Desidency Matteri University Fearlity of Medicine
1900 - 1909:	rediatrics Residency, Tottori University Faculty of Medicine
1991 – 1993:	Pediatric Neurology Residency, Division of Child Neurology, Tottori University
	Faculty of Medicine
1993 – 2003:	Research Associates, Division of Child Neurology, Tottori University Faculty
	of Medicine
1997 – 1998:	Research Fellow, Section of Epilepsy, Department of Neurology, Cleveland Clinic
	Foundation
2003 - 2004:	Assistant Professor, Division of Child Neurology, Tottori University Faculty
	of Medicine
2004 - present:	Associate Professor, Division of Child Neurology, Tottori University Faculty
	of Medicine

Main Publications

- 1) Okamoto R, Fujii S, Inoue T, Lei K, Kondo A, Hirata T, Okada M, Suzaki I, Ogawa T, **Maegaki Y**, Ohno K. Biphasic clinical course and early white matter abnormalities may be indicators of neurological sequela after status epilepticus in children. Neuropediatrics 2006; 37: (in press)
- 2) **Maegaki Y**, Kurozawa Y, Hanaki K, Ohno K. Risk factors for fatality and neurological sequelae after status epilepticus in children. Neuropediatrics 2005; 36: 186-192.
- 3) Ogura K, **Maegaki Y**, Koeda T. EEG evaluation of fixation-off sensitivity in eyelid myoclonia with absences. Pediatr Neurol. 2005; 33: 142-145.
- 4) Burioka N, Cornelissen G, **Maegaki Y**, Halberg F, Kaplan DT, Miyata M, Fukuoka Y, Endo M, Suyama H, Tomita Y, Shimizu E. Approximate entropy of the electroencephalogram in health awake subjects and absence epilepsy patients. Clinical EEG and Neuroscience 2005; 36: 188-193.
- 5) **Maegaki Y**., Bajm I., Terada K., Morris H. H., Bingaman W. E., Kohaya N., Takenobu A., Kadonaga Y., Lüders H. O. Somatosensory evoked high-frequency oscillations recorded directly from the human cerebral cortex. Clin. Neurophysiol. 2000; 111: 1916-1926.
- 6) Maegaki Y., Maeoka Y., Ishii S., Eda I., Ohtagaki A., Kitahara T., Suzuki N., Yoshino K., Ieshima A., Koeda T., Takeshita K. Central motor reorganization in cerebral palsy patients with bilateral cerebral lesions. Pediatr. Res. 1999; 45: 559-567.
- 7) Nanba Y., **Maegaki Y**. Epileptic negative myoclonus induced by carbamazepine in a child with BECTS. Pediatr. Neurol. 1999; 21: 664-667.

Hideto YOSHIKAWA

Education

1985:	M. D. Niigata University School of Medicine
1992:	Ph. D Toho University School of Medicine.

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Post-Graduate Training and Present Appointment

1985 – 1987:	Postgraduate trainee in Department of Pediatrics,	
	Niigata University Hospital, Niigata University School of Medicine, Niigata, Japan	
1987 – 1991:	Division of Child Neurology, Musashi Hospital, National Center of Neurology and	
	Psychiatry, Kodaira, Japan	
1991 – 1993:	Visiting Fellow: National Institute of Mental Health, Bethesda, USA	
1995 – 1997:	Nagaoka Institute of Severely Handicapped, Nagaoka, Japan	
199 – 2003:	Department of Pediatrics, Niigata City General Hospital, Niigata, Japan	
2003 – present:	Chief, Department of Neurology, Miyagi Children's Hospital, Sendai, Japan	

Main Publications

- 1) Yoshikawa H, Abe T. Acute respiratory distress syndrome in severely disabled children. Brain Dev 2005; 27: 395-399.
- 2) Tada H, Takanashi J, Barkovich AJ, Oba H, Maeda M, Tsukahara H, Suzuki M, Yamamoto T, Shimono T, Ichiyama T, Taoka T, Sohma O, **Yoshikawa H**, Kohno Y. Clinically mild encephalitis/ encephalopathy with reversible splenium lesion. Neurology 2004; 63: 1854-1858
- 3) **Yoshikawa H**, Yamazaki S. A study of intravenous midazolam for status epilepticus in children. J Jpn Epil Soc 2004; 22: 180-185.
- 4) Yoshikawa H, Abe T. Febrile convulsion in the acute phase of Kawasaki disease. Pediat Int 2004; 46: 31-32.
- 5) **Yoshikawa H**. EDTA-dependent pseudothrombocytopenia induced by valproic acid. Neurology 2003; 61: 579-80
- 6) **Yoshikawa H**, Watanabe T, Abe T. Hypouricemia in severely disabled children I : -influence of valproic acid and bed ridden state-. Brain Dev 2003; 25: 186-190.
- 7) Yoshikawa H, Yamazaki S, Watanabe T, Abe T. Vitamin K deficiency in severely disabled children. J Child Neurol 2003; 18: 93-97
- 8) Tanaka H, Nakajima M, Fujisawa M, Kasamaki M, Hori Y, **Yoshikawa H**, Kitagawa S. Rapid determination of total bromide in human serum using an energy-dispersive X-ray spectrometer. Biol Pharm Bull 2003; 26: 457-461.
- 9) Yoshikawa H, Yamazaki S, Watanabe T, Abe T. Study of influenza-associated encephalitis/ encephalopathy in children during the 1997-2000 influenza seasons. J Child Neurol 2001; 16: 885-890.

Hoglund P, Sormaala M, Haila S, Socha J, Rajaram U, Scheurlen W, Sinaasappel M, De Jonge H, Holmberg C,

- Yoshikawa H, Kere J. Identification of seven novel mutations including the first two genomic rearrangements in SLC26A3 mutated in congenital chloride diarrhea. Hum Mutat 2001; 18: 233-242.
- 11) **Yoshikawa H**, Yamazaki S, Abe T, Oda Y. Midazolam as a first-line agent for status epilepticus in children. Brain Dev 2000; 22: 239- 242.
- 12) **Yoshikawa H**, Yamazaki S, Abe T, Oda Y. Liposteroid therapy for refractory seizures in children. J Child Neurol 2000; 15: 702-704.
- 13) **Yoshikawa H**, Abe T, Oda Y. Extremely acute phenytoin-induced peripheral neuropathy. Epilepsia 1999; 40: 528-529.
- 14) Yoshikawa H, Watanabe T, Abe T, Oda Y. Clinical diversity in acute necrotizing encephalopathy. J Child Neurol 1999; 14: 249-255.

Shlomo SHINNAR

Present Position

9th ISS

9th ISS

Professor of Neurology and Pediatrics, Hyman Climenko Professor of Neuroscience ResearchmDirector, Comprehensive Epilepsy Management Center, Montefiore Medical Center, Albert Einstein College of Medicine,Bronx, New York



Shlomo Shinnar, MD, PhD is Professor of Neurology and Pediatrics, Hyman Climenko Professor of Neuroscience Research and director of the Comprehensive Epilepsy Management Center at Monte-fiore Medical Center and the Albert Einstein College of Medicine, Bronx, NY.

Dr Shinnar received a bachelor of arts degree, summa cum laude, in physics (1971) from Columbia College, New York. From 1971 to 1978, he was a predoctoral fellow with the National Institutes of Health (NIH) Medical Scientist Training Program at Albert Einstein College of Medicine, where he received a doctor of philosophy degree (1977) in neurophysiology and a doctor of medicine degree (1978). From 1978 to 1980, Dr Shinnar completed an internship and was an assistant resident and a fellow in general pediatrics, Department of Pediatrics, at the Johns Hopkins Hospital, Baltimore, MD. He was an assistant resident and resident in neurology and a fellow in child neurology from 1980 to 1983 at the Johns Hopkins Hospital. He has been at Montefiore Medical Center and the Albert Einstein College of Medicine since 1983.

Dr Shinnar is board-certified by the American Board of Psychiatry and Neurology (in neurology, with special competence in child neurology and added qualification in clinical neurophysiology) and the American Board of Pediatrics. He is a Fellow of the American Academy of Neurology and the American Academy of Pediatrics and a member of the American Neurological Association and the Society for Pediatric Research. He has been active in the American Epilepsy Society and the Epilepsy Foundation of America. He has also been active in local epilepsy societies, including the Epilepsy Foundation of Southern New York and the Epilepsy Institute.

Dr Shinnar is well known for his research on a variety of topics relating to childhood seizures, including when to initiate and discontinue antiepileptic drug therapy, prognosis following a first seizure, prognosis following discontinuation of medications in children with seizures, status epilepticus, and febrile seizures. He has been the principal investigator and coinvestigator on a variety of NIHfunded research studies. He is the Principal Investigator of a large multicenter study "Consequences of Prolonged Febrile Seizures in Childhood". He is also a member of the executive committee and co-investigator of a large multicenter NIH funded study "Childhood Absence Epilepsy: Rx, PK-PD-Pharmcogenetics". He has also been involved in industry-sponsored trials of new medications. Dr Shinnar is a recipient of the Research Recognition Award of the American Epilepsy Society. He has authored over 150 papers and is the senior editor of the book *Childhood Seizures* and coeditor of the recently published *Febrile Seizures*. Dr Shinnar has served as a reviewer and editorial board member for a variety of journals and is currently on the editorial boards of *The Neurologist* and *Pediatric Neurology*. He has frequently lectured at both national and international conferences.

Joon Soo LEE

Present Position :

Associate Professor, Division of Pediatric Neurology, Department of Pediatrics, Yonsei University College of Medicine. Chief of Handicapped Children's Institute



Education :

1980.3 - 1986.2:	Medical Degree, College of Medicine, Yonsei University		
1999.11 - 2001.10:	Research fellowship for PET scan and Epilepsy PET center, Children's Hospital		
	of Michigan, Wayne State University, Detroit, Michigan, USA.		
1999.3 – 2003.2:	Doctor Degree, College of Medicine, Ajou University, Suwon, Korea		

Membership

The Korean Medical Association, The Korean Pediatrics Society, The Korean Child Neurology Society, The Korean Epilepsy Society, The American Epileptic Society

Selected Articles :

- 1) Lee JS, Park JH, Coe CJ. Clinical characteristics of complex partial seizure a temporal versus a frontal lobe onset. J Kor Child Neurol Soc 1998; 6 : 769-774.
- 2) Lee JS, Juhasz C, Kaddurah AK, Chugani HT. Patterns of cerebral glucose metabolism in early and late stages of Rasmussen's syndrome. J Child Neurol. 2001; 16(11) : 798-805.
- 3) Lee JS, Asano E, Muzik O, Chugani DC, Juhasz C, Pfund Z, Philip S, Behen M, Chugani HT. Sturge-Weber syndrome: correlation between clinical course and FDG PET findings. Neurology. 2001; 57(2) : 189-95.
- 4) Pfund Z, Chugani DC, Muzik O, Juhasz C, Behen ME, Lee JS, Chakraborty P, Mangner T, Chugani HT. Alpha[11C] methyl-L-typtophan positron emission tomography in patients with alternating hemiplegia of childhood. J Child Neurol. 2002; 17(4): 253-60.
- 5) Lee JS, Pfund Z, Juhasz C, Behen ME, Muzik O, Chugani DC, NigrO MA, Chugani HT. Altered regional brain glucose metabolism in Duchenne muscualr dystrophy : a PET study. Muscle & Nerve 2002; 26 : 506-512.
- 6) Lee JS, Positron emission tomography: Application in pediatric epilepsy. J Korean Epilep Soc 2002; 6(2): 89-103.
- 7) Lee YM, Noh BH, Hur YJ Hur, Eun SH, Kang HC, **Lee JS**, Results of surgical treatments on intractable epilepsy with infantile spasm. J Korean Epilep Soc 2005; 13(2) : 162-171.
- 8) Kang DC, Lee YM, Lee JS, Kim HD, Coe CJ, Prognostic Factors of Status Epilepticus in Children. YMJ 2005; 46(1) : 27-33.



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Lucia FUSCO

Current Position:

Dirigente Medico I Livello (equivalent to Associate in Pediatric Neurology), Bambino Gesù Children's Hospital, Scientific Institute, Piazza S. Onofrio, 4 - 00165 Rome, Italy



Investigational Interests:

pediatric epilepsy and neurology, video/EEG monitoring of epileptic seizures, refractory pediatric epilepsy

Education

Medical Degree1973-1979Rome "La Sapienza" Univ.110/110 cum laudeSpecialization in Neurology1979-1983Rome "La Sapienza" Univ.70/70 cum laudePhilosophy Doctor Neuroscience1984-1989Firenze UniversityPh. D. NeuroscienceTeacher at University Updating Course on Epileptology and Electroencephalography since 1988.Member of Dierctory of Italian League Against Epilepsy (LICE) 2002-2005

Recent Publications:

- 1) **Fusco L**. and Specchio N. Non-epileptic paroxysmal manifestations during sleep in infancy and childhood. *Neurol Sci. 2005 Dec; 26(Supplement 3): s205-s209*
- 2) **Fusco L**. and Vigevano F. Indications for surgical treatment of epilepsy in childhood: a clinical and neurophysiological approach. *Acta Paediatr Suppl. 2004 May; 93(445): 28-31.*
- 3) Granata T, **Fusco L**, Gobbi G, et al. Experience with immunomodulatory treatments in Rasmussen's encephalitis. *Neurology. 2003* Dec 23; 61(12): 1807-1810.
- 4) Vigevano F, **Fusco L**, Lo Russo G, Broggi G. Epilepsy and malformations of cortical development *Epileptic Disord. 2003* Sep; 5 Suppl 2: S7-8.
- 5) Pachatz C, **Fusco L**, Vigevano F. Epileptic spasms and partial seizures as a single ictal event *Epilepsia*. 2003 May; 44(5): 693-700.
- 6) Dedek K, Fusco L, Teloy N, Steinlein OK. Neonatal convulsions and epileptic encephalopathy in an Italian family with a missense mutation in the fifth transmembrane region of KCNQ2. *Epilepsy Res. 2003* Apr; 54(1): 21-7.
- 7) Chiapparini L, Granata T, Farina L, Ciceri E, Erbetta A, Ragona F, Freri E, Fusco L. Diagnostic imaging in 13 cases of Rasmussen's encephalitis: can early MRI suggest the diagnosis? *Neuroradiology. 2003* Mar; 45(3): 171-83. Epub 2003 Feb 12.
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Nicola SPECCHIO

Education and Qualifications

- 2004: Attending a PhD on Neuroscience "Department of Neurological and Psychiatric Science, University of Bari, Italy"
- 1999 2004: Neurological Post-Graduate school. "Department of Neurological and Psychiatric Science, University of Bari, Italy".
- 1993 1999: Degree in Medicine: faculty of Medicine, University of Bari, Italy.

Present Position

Division of Neurology, Children's Hospital Bambino Gesù, Rome, Italy

Selected Publications

- 1) Striano P, Bordo L, Lispi ML, **Specchio N**, Minetti C, Vigevano F, Zara F. A novel SCN2A mutation in family with Benign Familial Infantile Seizures. Epilepsia 2006; 47(1): 218-220.
- 2) de Tommaso M, Di fruscolo O, Sciruicchio V, **Specchio N**, Cormio C, De Caro MF, Livrea P. Efficacy of levetiracetam in huntington disease. Clin Neuropharmacol 2005; 28(6): 280-284.
- 3) Fusco L, **Specchio N**. Non-epileptic paroxysmal manifestations during sleep in infancy and childhood. Neurol Sci, 2005; 26 (s3): 205-209.
- 4) **Specchio N**, Kahane P, Pasquier B, Tassi L and Guerrini R. resective surgery for epileprogenic dysembryoplastic neuroepithelial tumor in hemimegalencephaly. Neurology, 2005; 65 (5): 777-778.
- 5) Mimrod D, Specchio LM, Britzi M, Perucca E, **Specchio N**, La Neve A, Soback S, Levy RH, Gatti G, Doose DR, Maryanoff BE, and Bialer M. A Comparative Study of the Effect of Carbamazepine and Valproic Acid on the Pharmacokinetics and Metabolic Profile of Topiramate at Steady State in Patients with Epilepsy. Epilepsia, 2005; 46(7): 1046-1054.



Yoshiko HIRANO

Education

2003:



M. D. Tokyo Women's Medical University



Post-Graduate Training and Present Appointment

2003 - 2004:	Junior resident in Pediatrics,	
	Tokyo Women's Medical University	
2004 - 2005:	Medical staff in NICU,	
	Chiba City Kaihin Hospital	
2005 - 2006:	March: Senior resident in Pediatrics,	
	Tokyo Women's Medical University	
From 2006 April:	PhD course in Pediatrics, Tokyo Women's Medical University,	
	Graduate School of Medicine	

Hitoshi YAMAMOTO

Education

1974 - 1979:	St. Marianna University School of Medicine, Kawasaki, Japan
	M. D., 1979
1989:	St. Marianna University School of Medicine, Kawasaki, Japan
	Ph. D., 1989

Post-Graduate Training and Present Appointment

- 1979 1981: Resident in Pediatrics, St. Marianna University School of Medicine
- 1981 1984: General Pediatrics Fellow, St. Marianna University School of Medicine
- 1990 1991: Research Fellow, Department of Neuroscience, University of California, San Diego, California
- 1994 2004: Instructor, Department of Pediatrics, St. Marianna University School of Medicine
- 2004 present: Associate Professor, Department of Pediatrics, St. Marianna University School of Medicine

Selected Publications

- 1) **Yamamoto H**, Yoda T, Murakami H, et al. Treatment with lidocaine for status epilepticus in lowbirth-weight infants and neonates. Tenkan Kenkyu (in Japanese) 2004; 22: 96-100.
- 2) **Yamamoto H**, Yamano T, Niijima S, Kohyama J, Yamanouchi H. Spontaneous improvement of intractable epileptic seizures following acute viral infections. Brain Dev 2004; 26: 377-379.
- Miyamoto Y, Yamamoto H, Murakami H, Kamiyama N, Fukuda M. Studies on cerebrospinal fluid ionized calcium and magnesium concentrations in convulsive children. Pediatrics Int 2004; 46: 394-397.
- Yamamoto H, Sasamoto Y, Miyamoto Y, Murakami H, Kamiyama N. A successful treatment with pyridoxal phosphate for West syndrome in hypophosphatasia. Pediatr Neurol 2004; 30: 216-218.
- 5) Miyamoto Y, **Yamamoto H**, Fukuda M, et al. Newly developed liposteroid therapy for the patients with intractable epilepsy. Nihonshonikagakkaizasshi (in Japanese) 2004; 108: 993-996.
- 6) **Yamamoto H**, Imai K, Kamiyama N. Three cases of primary microcephaly associated with epilepsy. Tenkan Kenkyu (in Japanese) 2004; 22: 201-205.



9th ISS

Hideo YAMANOUCHI

Education

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1985:	M. D. Mie	University School of Medicine
[_] 1994:	Ph. D.	Gunma University School of Medicine



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Postdoctoral Training and Present Appointment

1985 – 1987:	Resident, Pediatrics, Gunma University School of Medicine
1989 – 1991:	Resident, Division of Child Neurology, National Center of Neurology
	and Psychiatry, Tokyo, Japan
1991 – 1996:	Staff, Pediatric Neurologist, Division of Child Neurology, National Center
	of Neurology and Psychiatry
1997 – 1999:	Assistant Professor, Gunma University School of Medicine, Gunma, Japan
1999 – 2004:	Staff, Pediatric Neurologist and Lecturer, Dokkyo University School of Medicine,
	Tochigi, Japan
2004 – :	Staff, Pediatric Neurologist and Associate Professor, Dokkyo University School of
	Medicine, Tochigi, Japan

Memberships

1985 Member, Japanese Society of Pediatrics	
1987 Member, Japanese Society of Child Neurology	
1989 Member, Japan Epilepsy Society	
1990 Member, Japanese Society of Neuropathology	
2001 Committee, Infantile Seizure Society	
2002 Affiliate Member, Child Neurology Society, USA	
2003 Member, International Child Neurology Association	
2004 Corresponding Active Member, American Academy of Neurology	

Publications

- 1) Yamanouchi H, Kawaguchi N, Mori M, Imataka G, Yamagata T, Hashimoto T, Momoi MY, Eguchi M. Acute infantile encephalopathy predominantly affecting the frontal lobes. Pediatr Neurol 2006; 34: 93-100.
- 2) Yamanouchi H. Activated remodeling and N-methyl-D-aspartate (NMDA) receptors in cortical dysplasia. J Child Neurol 2005; 20: 303-307.
- 3) Yamanouchi H. Imataka G, Nakagawa E, Nitta A, Suzuki N, Hirao J, Suzumura H, Watabe H, Arisawa O, Eguchi M. An analysis of epilepsy with chromosomal abnormalities. Brain Dev 2005; 27: 370-377.

Year	Theme	Invited Faculty	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 & Deveopment 2005; 27 (2) : 79-140
2004	Neuronal Migration Disorders and Childhood Epilepsies	Battaglia GS, Crino PB, Curatolo P, Fushiki H, Golden JA, Granata T, Guerrini R, Kakita A, Kato M, Kure S, Leventer RJ, Matsuda H, Mochida GH, Nakajima K, Otsubo H, Shimizu H, Shimozawa N, Takanashi J, Takano T, Tanaka T, Woermann FG, Yamano T, Yamanouchi H, Yoshioka M	Jounal of Child Neurology 2005; 20 (4) : 273-397
2005	Epileptic Syndromes in Infancy and Early Childhood	Scher MS, Plouin P, De Vivo DC, Yanagihara K, Ohtahara S, Moshe SL, Kasteleijn-Nolst Trenite DGA, Fejerman N, Lux AL, Kato M, Yamatogi Y, Nordli DR Jr, Ohtsuka Y, Craiu D, O'Regan ME, Engel J Jr, Berg AT, Inoue Y, Andermann F, Wolf P, Specchio N, Okumura A, Capovilla G, Lee WL, Kato N, Tanabe T, Kim DW, Hirsch E, Sankar R, Hayashi K, Nakayama J, Ito M, Scheffer I, Fujiwara T, Hirose S, Kanai K, Ohmori I, Yamakawa K, Awaya Y, Yamanouchi H	Epilepsy Research Supplement, 2006 (in press)

The 10th Annual Meeting of the Infantile Seizure Society

President	:	Dr Takao Takahashi Professor, Department of Pediatrics, Keio University School of Medicine, Tokyo, Japan
Date	:	Early April, 2007 (Details to be determined)
Venue	:	Tokyo, Japan (Details to be determined)
Main theme	:	Biology of seizure susceptibility during neonatal and infantile period
Objectives	:	Explorations thorough comprehensive presentations and thorough discussion on such issues as morphogenesis, receptors and neurotransmitters, ion channels and pharmacodynamics are in prospect.
Contact	:	10th ISS Secretariat c/o Department of Pediatrics, Keio University, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan Phone : +81-3-5363-3815 Fax : +81-3-3356-7022 E-mail : ttakahashi@z3.keio.jp