London on View

The 5th London-Innsbruck Colloquium on Status Epilepticus and Acute Seizures

9-11 April 2015
London, United Kingdom

Final Programme

www.statusepilepticus2015.eu

Great Hall, Sherfield Building,
Imperial College,
South Kensington Campus,
London SW7 2AZ, United Kingdom

PATRONS

Paracelsus Medical University
Christian Doppler Klinik
Ignaz Harrer Strasse 79
A-5020 Salzburg, Austria

University College London
Institute of Neurology
Queen Square
London WC 1N 3BG
United Kingdom

CHAIRS

Simon Shorvon, London, United Kingdom
Eugen Trinka, Salzburg, Austria

Dear friends and colleagues,

Eugen Trinka

Simon Shorvon

It is our sincere pleasure to welcome you all to London, to this the 5th London-Innsbruck Colloquium on Status Epilepticus and Acute Seizures.
These meetings have taken place biennially since 2007, and have become an important feature of the epilepsy calendar.

This year, the conference will focus on the clinical and experimental nature of status epilepticus and novel aspects of its treatment. It is our intention over the 3 days of the conference to have intensive and interactive discussion on the cutting edge of research and clinical practice in the field of status epilepticus. We hope to feature current basic and clinical research and to provide up-to-date reviews of the field. The aim of the meeting is to stimulate thought and discussion, and to lead to improvements in the treatment and outcome of this condition.

We have deliberately left space in the programme for the audience to question and to challenge - for we believe, as a fundamental pillar of the Colloquia, that academic debate is at the heart of all learning and discovery. We hope you will all join in this endeavour and contribute to what we hope will be a lively and instructive meeting.

Finally, some acknowledgements are in order. First, we would like to thank our conference organizing team, led by Mrs Ina Kähler, from PCO Tyrol Congress for their tremendous work. Also, the academic activities of this conference would not have been possible without the generous support of our sponsors listed at the back page of this booklet, and we offer our sincere thanks to them all. We are grateful too for the patronage of this conference by University College London and Paracelsus Medical University Salzburg.

With very best regards

Eugen Trinka and Simon Shorvon
Co-Chairs, 5th London-Innsbruck Colloquium on Status Epilepticus and Actue Seizures

Conference venue

Great Hall, Sherfield Building
Imperial College, South Kensington Campus
Londown SW7 2AZ, United Kingdom

Registration Desk at Sherfield Building

The registration will be located in the entrance area of the Sherfield Building, close to the Queen's Tower Rooms
Opening hours are as follows:

Thursday, 9 April	7:30 – 17:30
Friday, 10 April	7:45 – 18:00
Saturday, 11 April	8:15 – 16:15

Congress Organisers

PCO Tyrol Congress
Congress und Messe Innsbruck GmbH
Ms. Ina Kähler and Ms. Sarah Fechner
Rennweg 3
6020 Innsbruck, Austria
T: +43-(0)512-575600, F:+43-(0)512-565707
E: se2015@cmi.at
I: www.pco-tyrolcongress.at, www.cmi.at

Trade Exhibition

A trade exhibition of pharmaceutical companies and manufacturers of medical equipment is held in the Queen's Tower Rooms.

Exhibition Organisers

S12! studio 12 GmbH
Mr. Ralph Kerschbaumer
Kaiser Josef Straße 9
6020 Innsbruck, Austria
T: +43-(0)512-890438, F: +43-(0)512-890438-15
E: office@studio12.co.at

Certificate of Attendance

All registered delegates receive an official certificate of attendance together with their registration documents.

Cloakroom

The cloakroom is located on the first floor of the Sherfield Building.

Coffee breaks and refreshments

Coffee and tea will be served during the official coffee breaks. Lunch will also be provided. All refreshments are served in the exhibition area.

Smoking

Smoking is prohibited inside the Sherfield Building.

City Transportation

Arriving by London Underground

From South Kensington Station, the campus is only a five minute walk. The College is located next to the Science Museum.

Arriving by bus

South Kensington Campus is easily accessible by bus. A number of routes pass within easy walking distance of the campus.

Currency

The official currency in the United Kingdom is the Pound. Major credit cards are accepted in most hotels, shops and restaurants. Automatic teller machines (ATMs) are available throughout the city.

Name Badges

All registered participants receive a name badge together with their registration documents. Please make sure to wear your badge at all times while attending the meeting, exhibition and social events.

Liability and Insurance

Neither the organisers, nor the congress secretariat or other suppliers accept liability for personal injuries or loss or damage of property belonging to congress delegates, either during or as a result of the Congress. It is recommended that participants arrange for their own personal health, accident and travel insurance.

Social Programme

Conference Dinner at the Royal College of Physicians (RCP)

Food nourishes the brain and the soul, and at this the 2015 meeting, a rather splendid reception and dinner will be held at the Royal College of Physicians. In addition, there will be an opportunity also to visit the famous building of the College, see items from the College's museum and library, and also to view the temporary exhibition of paintings of medicinal plants.
Tickets are at EUR 55,00 p.p.
Pre-booking is required as tickets are limited!

Information for speakers

The Great Hall is equipped with a data projector and a PC for PowerPoint presentations. Please make sure to bring your PowerPoint presentation on a USB-stick to the media check well in advance, 2 hours prior to the start of your session at the very latest.
Do not bring your own laptop for the presentation.
In case your presentation contains video sequences, please ensure to pack them with a standard codec and do not store them in a Quick Time format since this may not be compatible with PowerPoint presentations.

In order to be able to keep the time schedule, please make sure not to exceed the allotted speaking time.

Information for poster presenters

The poster session is held on Friday, 10th April from 11:55 – 14:00 in the Queen's Tower Rooms (Sherfield Building).

POSTER FORMAT:
Your poster should not exceed 90 cm in width and 150 cm in height (portrait NOT landscape format). Mounting material will be provided on site.
All posters will be displayed during the entire congress and should be mounted on 9th April in the morning. Posters have to be displayed during the whole congress and have to be taken down on Saturday 11th April by the end of the colloquium. Please note that all posters which have not been taken down by their presenters will automatically be removed and discarded.

POSTER PRESENTATION DETAILS:
During the session you or one of your co-authors must be at your poster site and be prepared to answer questions.

THURSDAY APRIL 9TH 2015

08.30 - 12.30	**THE NATURE OF SE: EXPERIMENTAL ASPECTS**
	Chair: D. Kullmann (United Kingdom) and J. Kapur (USA)
08.30 - 08.40	**Welcome and introduction** S. Shorvon (United Kingdom) and E. Trinka (Austria)
08.40 - 09.15	**Is hypoxia important in status epilepticus?** G. Biagini (Italy)
09.15 – 09.50	**Structural and functional changes in astrocytes following status epilepticus** K. Wilcox (USA)
09.50 - 10.20	**Coffee Break**
	Chair: D. Lowenstein (USA) and A. Rossetti (Switzerland)
10.20 – 10.55	**What are the physiological bases of GPEDs and other EEG patterns in status epilepticus?** M. van Putten (The Netherlands)
10.55 - 11.30	**Is spreading depression important in status epilepticus?** J. Dreier (Germany)
11.30 - 12.05	**What does burst suppression really mean?** F. Amzica (Canada)
12.05 – 12.30	**Lunch**

12.30 – 13.30 **SATELLITE SYMPOSIUM:**
STATUS EPILEPTICUS – FROM BENCH TO BEDSIDE – CHALLENGES FOR TRANSLATING NEW MECHANISMS INTO NEW TREATMENTS
(Sponsored by Industry)

Co-Chairs: E. Trinka (Austria) and S. Shorvon (United Kingdom)

12.30 – 12.35 **Introduction**
E. Trinka (Austria) and S. Shorvon (United Kingdom)

12.35 – 13.00 **Animal models of status epilepticus: perspectives on predictability and translation**
M. Walker (United Kingdom)

13.00 – 13.25 **Clinical trials for status epilepticus: perspectives on feasibility**
A. Rossetti (Switzerland)

13.25 – 13.30 **Concluding remarks**
E. Trinka (Austria) and S. Shorvon (United Kingdom)

13.30 – 14.00 **PANEL DISCUSSION**

Chair: M. Baulac (France)

The conference perspective on translating new mechanisms into new treatments

14.00 - 17.30 **THE NATURE OF STATUS EPILEPTICUS: CLINICAL ASPECTS**

Chair: H. Cross (United Kingdom) and R. Guerrini (Italy)

14.00 - 14.30 **Pathophysiology of mitochondrial disease causing status epilepticus**
S. Rahman (United Kingdom)

14.30 - 15.00 **Status epilepticus, inflammation and blood brain barrier disruption**
J. Gorter (The Netherlands)

15.00 - 15.30 **P2X receptor as a link between hyperexcitability and neuroinflammation in status epilepticus**
D. Henshall (Ireland)

15.30 - 16.00 **Coffee Break**

Chair: N. Bharucha (India) and C. Wasterlain (USA)

16.00 - 16.30 **Gene mutations associated with status epilepticus**
S. Shorvon (United Kingdom)

16.30 – 17.00 **Predicting the outcome of status epilepticus**
M. Leitinger (Austria)

17.00 - 17.30 **Expert Panel Discussion:**
The experimental and clinical nature of status epilepticus

Chair: E. Trinka (Austria)

M. Cook (Australia), R. Guerrini (Italy), J. Kapur (USA), D. Lowenstein (USA), A. Rossetti (Switzerland), C. Wasterlain (USA)

19.30 - 23.00 **RECEPTION AND DINNER**
(Royal College of Physicians)

FRIDAY APRIL 10TH 2015

08.30 - 12.30 **CLINICAL ASPECTS OF STATUS EPILEPTICUS**

Chair: M. Koepp (United Kingdom) and D. Lowenstein (USA)

08.30 - 09.05 **The nature of neonatal status epilepticus**
D. Dlugos (USA)

09.05 - 09.40 **Drug induced status epilepticus**
H. Cock (United Kingdom)

09.40 - 10.15 **Can anaesthetic treatment worsen outcome in status epilepticus?**
R. Sutter (Switzerland)

10.15 - 10.45 Coffee Break

Chair: T. Bleck (USA) and R. Guerrini (Italy)

10.45 - 11.20 **Systemic complications of status epilepticus**
S. Hocker (USA)

11.20 - 11.55 **Audit of treatment in refractory status epilepticus**
M. Ferlisi (Italy)

11.55 – 14.00 **CONFERENCE PHOTOGRAPH, POSTERS AND LUNCH**

14.00 – 15.00 **MINI-SYMPOSIUM: CANNABINOIDS AND STATUS EPILEPTICUS**

14.00 – 14.30 **Cannabinoid pharmacology in preclinical models of seizure, status and epilepsy**
B. J. Whalley (United Kingdom)

14.30 – 15.00 **Emerging clinical effects of cannabinoids in epilepsy**
H. Cross (United Kingdom)

15.00 - 15.30 Tea Break

15.30 - 17.15 **ELECTROGRAPHIC STATUS EPILEPTICUS**

Chair: R. Pressler (United Kingdom) and A. Rossetti (Switzerland)

15.30 - 16.00 **Electrographic status epilepticus in critically ill children: epidemiology and outcome**
N. Abend (USA)

16.00 - 16.30 **Outcome of electrographic status epilepitcus**
T. Loddenkemper (USA)

16.30 - 17.00 **Which EEG Patterns in Coma are nonconvulsive status epilepticus?**
E. Trinka (Austria)

17.00 – 17.15 **GPEDs and status epilepticus – a matter of frequency?**
M. Koutroumanidis (United Kingdom)

17.15 - 18.00 **DEBATE**

Chair: S. Shorvon (United Kingdom)

Motion: Should PEDs (and similar EEG Patterns) in post-anoxic status epilepticus be treated ?
Pro: L. Hirsch (USA)
Contra: P. Kaplan (USA)

SATURDAY APRIL 11TH 2015

08.45 - 12.00 **NOVEL ASPECTS IN THE DRUG TREATMENT OF STATUS EPILEPTICUS**

Chair: C. Wasterlain (USA)

08.45 – 9.00 **Invited lecture: System mechanisms of anti-epileptic protection**
V. Karlov (Moscow)

09.00 - 09.30 **Intranasal therapies of acute seizures**
R. Kälviainen (Finland)

09.30 - 10.00 **Intramuscular and rectal therapies of acute seizures**
I. Leppik (USA)

10.00 - 10.30 **SPD and valnoctamide**
M. Bialer (Israel)

10.30 – 11.00 **Coffee Break**

11.00 - 12.00 **MINI SYMPOSIUM: NEUROSTEROIDS**
(Sponsored by Industry)

11.00 – 11.30 **SAGE 689, a second generation neuroactive steroid for status epilepticus**
A. Robichaud (USA)

11.30 – 12.00 **SAGE 547, for super refractory status epilepticus; a clinical update**
S. Kanes (USA)

12.00 - 12.30 **LUNCH**

12.30 – 13.45 **SPECIAL SYMPOSIUM: SEIZURE CLUSTERS**
(Supported by an educational grant by Industry)

12.30 - 13.00 **Can we predict seizure clusters? - Insights from neurophysiology**
T. Loddenkemper (USA)

13.00 - 13.30 **Seizure clusters and serial seizures - a clinical entity or part of a continuum?**
M. Holtkamp (Germany)

13.30 - 13.45 Discussion

13.45 - 16.15 **NOVEL ASPECTS IN THE DRUG TREATMENT OF STATUS EPILEPTICUS**

Chair: J. Kapur (USA) and T. Bleck (USA)

13.45- 14.15 **New experimental therapies in pre-clinical development**
M. Walker (United Kingdom)

14.15 - 14.45 **Single v. combinational therapies in status epilepticus**
W. Löscher (Germany)

14.45 – 15.15 **A tale of two receptors: synergistic drug combinations for status epilepticus**
C. Wasterlain (USA)

15.15 – 15.45 **Propofol Hemisuccinate**
M. Rogawski (USA)

15.45 – 16.15 **Lacosamide**
A. Husain (USA)

16.15 **END OF COLLOQUIUM AND TEA**

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POSTER SESSION
Friday, 10th April 2015, 11:55 - 14:00
Queens Tower Rooms

Basic aspects of status epilepticus

P01

Propylparaben modifies hippocampal GABA and glutamate release during status epilepticus induced by pilocarpine administration in rat: correlations with epileptiform oscillations

César Emmanuel Santana Gómez, Sandra Orozco Suárez, Alan Talevi, Luis Bruno Blanch, Victor Manuel Magdaleno Madrigal, Manola Cuéllar Herrera, Luisa Rocha Arrieta (Mexico Df, Mexico)

P02

Transcranial focal electrical stimulation reduces the convulsive expression and glutamate release in hippocampus during pilocarpine-induced status epilpeticus in rats

Luisa Rocha, Cesar Santana-Gomez, David Alcantara-Gonzalez, Sandra Orozco-Suarez, Walter Besio (Mexico City, Mexico)

P03

Changes of hippocampal excitability after status epilepticus in immature rats

Petr Fabera, Hana Kubova, Pavel Mares (Prague 4, Czech Republic)

P04

Protein expression of phospho-lim kinase-1 in patients and an experimental rat model with intractable temporal lobe epilepsy

Hao Huang, Jinxian Yuan, Yangmei Chen (Chongqing, China)

P05

Glial waves during seizures – coupled or uncoupled with neurovascular activity?

Theodore Schwartz, Hongtao Ma, Andrew Daniel (New York, United States)

P06

Inflammation induced with LPS in developing rats reduces the range of morphological transformation of microglial cells in response to seizures evoked in adulthood

Krzysztof Janeczko, Emilia Kosonowska, Zuzanna Setkowicz (Krakow, Poland)

P07

The neuroactive steroid, SAGE-547, acutely arrests seizure activity in an animal model of pharmaco-resistant status epilepticus

James Doherty, Michael Quirk, Gabriel Belfort, Rebecca Hammond, Edward Christian, Carla Maciag, Steven Kanes, Albert Robichaud (Cambridge, Massachusetts, United States)

P08

The influence of ketogenic diet on the elemental and biochemical composition of hippocampal formation

Zuzanna Setkowicz, Agnieszka Skoczen, Krzysztof Janeczko, Agnieszka Patulska, Katarzyna Matusiak, Henryk Figiel, Paul Dumas, Christophe Sandt, Rolf Simon, Joanna Chwiej (Krakow, Poland)

P09

Nicotine partially suppresses evoked cortical discharges in adolescent rats exposed to hypoxia

Vladimir Riljak, Katerina Jandova, Jaroslav Pokorny (Prague, Czech Republic)

P10

Status epilepticus induction has prolonged effects on the efficacy of antiepileptic drugs in the 6 Hz seizure model

Karine Leclercq, Rafal M Kaminski (Braine L'Alleud, Belgium)

P11

Canine status epilepticus: response to fosphenytoin is similar to human status epilepticus

Edward (Ned) Patterson, Ilo Leppik, Lisa Coles, James Cloyd (Saint Paul, United States)

P12

Ultrasound stimulation improves behavioral outcome in an experimental model of mesial temporal lobe epilepsy

Daejong Jeon, Hilola Hakimova, Sangwoo Kim, Bumseok Jeong Bumseok Jeong, Kon Chu, Sang Kun Lee (Seoul, Republic Of South Korea)

Electroencephalographic aspects of status epilepticus

P13

Electrical status epilepticus during slow sleep in children with various forms of epilepsy

Raushan Kenzhegulova, Altynshash Jaxybaeva (Astana, Kazakhstan)

P14

Intracortical electroencephalography and multimodal neuromonitoring in comatose patients with acute brain injury: report of 3 cases

José L Fernández-Torre, Miguel Á Hernández-Hernández, David Mato-Mañas, Rubén Martínez-Láez, Guillermo García-Catalán, Enrique Marco de Lucas, Alfonso Vázquez-Barquero (Santander, Spain)

P15

Epileptiform activity in patients treated with therapeutic hypothermia after cardiac arrest: Is it status?

Carlos Santos Sanchez, Marta Agundez Sarasola, Xabier Mancisidor Solaberrie, Pedro Goiriena Seijo, Aitor Martin López, Tomas Perrez Concha, Izaskun Yurrebaso Santamaria (San Vicente De Barakaldo, Spain)

P16

Prediction of rhythmic and periodic EEG patterns and seizures on continuous EEG with early epileptiform discharges

Johannes Koren, Johannes Herta, Simone Draschtak, Georg Pötzl, Franz Fürbass, Manfred Hartmann, Tilmann Kluge, Christoph Baumgartner (Vienna, Austria)

P17

NeuroTrend: prospective validation of rhythmic and periodic pattern detection in the ICU

Johannes Herta, Johannes Koren, Franz Fürbass, Manfred Hartmann, Tillmann Kluge, Christoph Baumgartner, Andreas Gruber (Vienna, Austria)

P18

Ictal and Interictal EEG patterns in patients with non-convulsive and subtle-convulsive status epilepticus

Tushar Divakar Gosavi, Siew Ju See, Shih Hui Lim (Singapore, Singapore)

P19

New-onset refractory status epilepticus: etiology, clinical features and outcome

Nicolas Gaspard, Brandon Foreman, Vincent Alvarez, Christian Cabrera Kang, John Probasco, Amy Jongeling, Kevin Haas, Sarah Schmitt, Elizabeth Gerrard, Teneille Gofton, Suzette LaRoche, Lawrence Hirsch (Bruxelles, Belgium)

P20

Incidence of recurrent seizures in patients with LPDs (PLEDs) and non-convulsive seizures recorded on continuous EEG in the critical care setting

Vineet Punia, Stephen Hantus (Cleveland, United States)

P21

Dynamics and variability of burst suppression in pharmcological coma for refractory status epilepticus

Jingzhi An, Brandon Westover, Durga Jonnalagadda, Valdery Moura Junior, Patrick Purdon, Emery Brown (Cambridge, United States)

P22

Yield of continuous EEG using the 2012 ACNS terminology in outcome prediction after status epilepticus

Vincent Alvarez, Frank W. Drislane, M Brandon Westover, Barbara Dworetzky, Jong Woo Lee (Sion, Switzerland)

P23

Extreme delta brush, could be an ictal pattern in patients with anti-NMDA receptor encephalitis

Misericordia Veciana, Juan Luís Becerra, Pilar Fossas, Desiré Muriana, Gemma Sansa, Estebo Santamarina, Carles Gaig, Mar Carreño, Albert Molins, Concepció Escofet, Miguel Ley, Rosa Vivancos (L'Hospitalet De Llobregat, Bar, Spain)

P24

Forehead EEG electrode compared to full-head scalp EEG in 100 patients with altered mental state

Esa Mervaala, Susanna Westeren-Punnonen, Anu Muraja-Murro, Katja Myllymaa, Sami Myllymaa, Pasi Lepola, Reijo Lappalainen, Juha Töyräs, Leena Jutila, Anne-Mari Kantanen, Pekka Jäkälä, Reetta Kälviäinen (Kuopio, Finland)

Phenomenological aspects of status epilepticus

P25

Thai national data of status epilepticus: 9 years

Sineenard Pranboon, Somsak Tiamkao, Kaewjai Thepsuthammarat, Kittisak Sawanyawisuth (Khon Kaen, Thailand)

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POSTER ABSTRACTS

P01

Propylparaben modifies hippocampal GABA and glutamate release during status epilepticus induced by pilocarpine administration in rat: correlations with epileptiform oscillations

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Previous studies indicate that the administration of propylparaben (PPB; an antimicrobial agent with low toxicity and widely used) reduces the seizure activity induced by pentylenetetrazole and inhibits voltage-dependent sodium channels in cardiomyocytes of the rat. The aim of the present study was to determine if PPB modifies the Status Epilepticus (SE) induced by pilocarpine, and their correlation with electrographic activity and GABA-glutamate release in hippocampus. Male Wistar rats previously implanted with a bipolar electrode coupled to a guide cannula into the right ventral hippocampus were subjected to microdialysis experiments during which SE was induced by pilocarpine administration (300 mg/kg, i.p., SE group, n=6). Diazepam (DZP 2.5 mg/kg, i.m.) was applied 2 h after the SE establishment. The electrographic activity of hippocampus was analyzed using fast fourier transform. The SE+PPB group (n=6) was manipulated as described above, except that animals received PPB (178 mg/kg, i.p.) 1 h after DZP. Animals were sacrificed 24 h after the SE and the brain was used to determine the site of electrode/cannula implantation (Nissl staining). SE and SE+PPB groups showed similar basal levels of GABA and glutamate (0.34±0.06 μM and 1.20±0.29 μM, respectively) with prevalence of low frequency oscillations (0.1-4 Hz). The SE was established at 43.2±2.5 min after pilocarpine injection and was associated with the progressively increase of GABA and glutamate release. This effect was evident at 47 min after the establishment of the SE, (GABA, 135%; glutamate, 140%), and was associated with the prevalence of gamma and ripples oscillations. Although DZP administration reduced the convulsive activity and the ripple oscillations, GABA and glutamate release remains elevated (270% and 330% respectively; $p<0.05$). In contrast to SE group, the SE+PPB group showed a progressive decrease of the GABA and glutamate levels after PPB administration (155% and 177%, respectively; $p<0.001$), effect associated with a significant decrease in the epileptiform electrographic activity (with prevalence of beta oscillations). We conclude that the administration of PPB at the end of the SE reduces the epileptiform activity as well as the GABA and glutamate release in hippocampus.

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P02

Transcranial focal electrical stimulation reduces the convulsive expression and glutamate release in hippocampus during pilocarpine-induced status epilpeticus in rats

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In previous studies we demonstrated that noninvasive transcranial focal electrical stimulation (TFS) in association with sub-effective doses of diazepam reduces the Status Epilepticus (SE)-induced neuronal damage. However, it is unclear if this neuroprotective effect is consequence of the decrease in the glutamate release. The aim the present study was to evaluate the effects of TFS on glutamate release in hippocampus during the pilocarpine-induced SE. Male Wistar rats were implanted with a guide cannula attached to a bipolar electrode into the right ventral hippocampus. A concentric ring electrode pole was placed on the skull surface, as close to 5 mm behind the bregma as possible. Animals were subjected to a microdialysis experiment during which SE was induced by pilocarpine administration (300 mg/kg, i.p.). A group of animals was manipulated as described above, except that five minutes after the establishment of the SE, TFS was continuously applied during 2 h (300 Hz, 200 μs biphasic square pulses at 100 μA, for 2 h). The dialysates were recovered throughout the microdialysis experiment and processed with high resolution liquid chromatography procedure to determine glutamate concentrations. The animals were sacrificed at the end of the experiments and the brain was used to verify the implant site with Nissl staining. Under basal conditions, the levels of glutamate were 0.98 ± 0.05 μM. After pilocarpine administration, the rats showed head myoclonus (15.2 ± 3.9 min), forelimb clonus (33.6 ± 6.1 min), rearing (33.7 ± 5.5 min) and wet dog shakes (37.9 ± 2.49 min). When the SE was established (43.09 ± 2.49 min), the release of glutamate demonstrated a significant increase (141%), a situation that was evident at the end of the experiment (270%), 5 hours after pilocarpine injection. The TFS application during the SE reduced the behavioral and hippocampal electrographic convulsive activity, a situation associated with glutamate levels similar to basal conditions. TSF decreased the convulsive expression and the hippocampal glutamate release associated to SE. It is possible that this effect plays a significant role in the neuroprotection induced by TFS.

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P03

Changes of hippocampal excitability after status epilepticus in immature rats

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Status epilepticus (SE) induced in 12-day-old rats led after a long latency to development of spontaneous seizures. Majority of spontaneous seizures is generated in hippocampus therefore we started to study hippocampal excitability after SE.

Lithium-pilocarpine SE was elicited in 12-day-old rats and hippocampal epileptic afterdischarges were studied in 15-, 18-, 25- and 32-day-old rats with stimulation and recording electrodes implanted into dorsal hippocampus. Control animals received saline instead of pilocarpine. All groups were formed by 12-15 animals. Stimulation of hippocampus (2-s series of 60-Hz pulses of 1-ms duration) was performed by constant current stimulator. Threshold intensities were found and then the rats were stimulated with a suprathreshold intensity six times at 20-min intervals. Thresholds and duration of ADs were evaluated.
Threshold for elicitation of HiAD was significantly higher in 15-day-old SE rats than in controls. The two older groups did not exhibit any difference between SE and control group but 32-day-old rats exhibited a change opposite to P15 rats: threshold intensity was significantly lower in SE rats than in controls. Corresponding changes were found in AD duration after repeated stimulations – shorter ADs were recorded in P15 SE rats whereas ADs were significantly longer in P32 SE rats in comparison with controls. Recurrent ADs were not present in P15 rats, their incidence in P18 SE rats was very low in comparison with controls but rADs in P32 SE animals were more frequent than in controls.

Our data demonstrated that during 20 days after SE elicited at P12 complex changes of hippocampal excitability took place. P32 rats demonstrated higher excitability of dorsal hippocampus than their age-matched controls. This increased excitability might be a background of epileptogenesis after SE.

Study was supported by grants of the Grant Agency of the Czech Republic 15-16605S and P304/12/G069 and a project of the ASCR 67985823.

P04

Protein expression of phospho-lim kinase-1 in patients and an experimental rat model with intractable temporal lobe epilepsy

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Lim kinase-1 (LIMK1) plays a critical role in dendritic spine morphogenesis and brain function. Phospho-Lim kinase-1 (p-LIMK1), the active form of LIMK1, might be involved in the pathogenesis of human temporal lobe epilepsy (TLE). The protein expression pattern of p-LIMK1, in intractable TLE, however, is unknown. Here we used immunohistochemistry and Western blot assay to measure p-LIMK1 protein expression in 30 temporal neocortex tissue samples from intractable TLE patients, 15 histologically normal temporal neocortex tissue samples from trauma patients without epilepsy, in the hippocampi of lithium chloride/pilocarpine-induced TLE rats and in uninduced controls. We found that p-LIMK1 was expressed mainly in the cytoplasm of neurons. The protein expression of p-LIMK1 was significantly higher in the TLE patients and rats than in the control groups. p-LIMK1 protein may be involved in the pathogenesis of intractable TLE in humans and rat models.

P05

Glial waves during seizures – coupled or uncoupled with neurovascular activity?

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Background: Neuronal and glial activity are thought to coordinate regional blood flow through a complex sequence of events. During normal sensory processing, these events appear to be coupled in space and time. Using a 4-AP injection into rat cerebral cortex and simultaneous voltage sensitive and intrinsic signal (IS) wide-field imaging, we have previously shown that ictal events are coupled in space, but not time, with perfusion. Although glia are a key component in neurovascular coupling, wide-field imaging of glial waves during seizures has not been investigated.

Methods: Using calcium dyes, either OGB-1, which can be filtered to image glia (< 1 Hz) or neuronal activity (> 1Hz), or the calcium dye Rhod-2, which stains only astrocytes, along with IS and local field potentials, we were able to measure each compartment of the neurovascular unit through a wide area of in vivo rat neocortex during seizure onset and evolution.

Results: A clear glial wave which began focally and spread across the cortex occurred simultaneous with each ictal event. However, glial waves propagated 43% further (4.3±1.3 mm) than CBV changes (3.0 ± 1.0 mm, t-test, p=0.0013). Despite widely varying seizure durations (10-70s, 43.5±17.6 s), the duration of astrocytic activation remained more constant (10-40s, 23.6±6.5 s) and did not significantly correlate with the duration of the seizures (n = 25 seizures from 4 rats, r = 0.28, p = 0.18). The hemodynamic change, on the other hand, lasted longer than both the astrocytic and neuronal activity in all trials (54.5±17.7 s, p <0.01). Moreover, glial waves were significantly delayed in onset compared with hemodynamic waves (2.4±1.1 s versus 0.8±1.0s respectively, p<0.01). Our results suggest that during ictal events, each compartment in the neurovascular unit displays a unique spatiotemporal onset and evolution.

Conclusions: Although clearly coupled in a macro-global scale ie. similar number of events in a similar region of cortex, they are uncoupled on a micro-detailed scale. In spite of rapidly propagating multidirectional subthreshold neuronal waves of varying duration, glial activity is characterized by a more homogeneous slowly propagating wave that extends well beyond the limits of the neuronal or perfusion changes, having a more constant predictable duration. These results call into question the putative essential role of astrocytes in ictal neurovascular coupling.

P06

Inflammation induced with LPS in developing rats reduces the range of morphological transformation of microglial cells in response to seizures evoked in adulthood

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In the brain, inflammation occurs following different damages including epileptic seizures. It was proven that pro-inflammatory cytokines, like IL-1beta or TNFalfa, increase neuronal excitability and can initiate spontaneous seizures or epileptogenesis. Recent studies indicate that the effects can be attenuated or even abolished in animals subjected to inflammation-inducing treatments at earlier developmental stages. It was termed "preconditioning". Microglia are the major immunocompetent cell type in the brain showing a morphological continuum from resting to reactive forms. Following inflammation, multiple ramified processes of resting microglia become gradually shorter and the cells transform into macrophages. Parameters of the morphological changes were used here as indicators of the nervous tissue reactivity to seizures in adult rats experiencing inflammation at earlier stages of their postnatal development. Systemic inflammation was induced with liposaccharide (LPS) in 6- or 30-day-old rats. In two-month-old survivors of the inflammatory status, seizures were evoked with pilocarpine. Brain sections were immunostained for Iba1 to analyse morphology of microglial cells (circularity, solidity, surface area, critical radius, sum and mean of intersections, ramification index) in the hippocampal formation. In naïve rats, seizure-induced reactive transformations of microglial cells were reflected by changes in the above mentioned parameters of their morphology. However, in the adult rats pre-treated with LPS on their 6 or 30 postnatal days, the seizure-induced changes were significantly reduced and microglial morphology remained similar to normal. The results confirm previous reports that a moderate inflammation protects the nervous tissue from subsequent damages by reducing influences of pro-inflammatory factors on reactive glial cells. This work was supported by the Polish National Science Centre, grant UMO-2012/05/B/NZ4/02406.

P07

The neuroactive steroid, SAGE-547, acutely arrests seizure activity in an animal model of pharmaco-resistant status epilepticus

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Background: Status Epilepticus (SE) is a neurological emergency with a mortality rate estimated at 22% (DeLorenzo et al, 1995). Benzodiazepines are first-line treatments for SE (Brophy et al, 2012), although ineffective in approximately 30% of patients (Silbergleit et al, 2012). Neuroactive steroids (NASs) act as positive allosteric modulators across multiple $GABA_A$ receptor isoforms and thus may be less susceptible to acute pharmaco-resistance during SE. This study examined the efficacy of SAGE-547 (allopregnanolone) in reducing electrographic seizures in the lithium-pilocarpine rat model of pharmaco-resistant SE.

Methods: Male SD rats (~300g) implanted with screw electrodes over the frontal cortex and IV jugular vein catheters were administered lithium (127 mg/kg, IP) and pilocarpine (50 mg/kg, ip) to elicit SE. Test articles were administered immediately, 15 or 60 min after onset of SE.

Results: SAGE-547 produced a robust, dose dependent arrest of SE in this rodent model, measured by behavioral convulsion or abnormal EEG activity. SAGE-547 (5-15 mg/kg, iv) arrested SE when administered 15 minutes following SE induction. Exposure of SAGE-547 was 1912±359 nM in plasma and 2601±203 nM in brain at 15 minutes following iv bolus. SAGE-547 remained effective at 60 minutes after SE induction, a treatment latency that produces resistance to multiple antiepileptic pharmacotherapies, including benzodiazepines. Exposure levels were 880±146 nM in plasma and 1411±265 nM in brain.

Co-administration of SAGE-547 and pentobarbital was conducted to assess the effect of additional GABAergic agents on the efficacy of SAGE-547 in SE. When combined with a sub-active dose of pentobarbital, SAGE-547 effectively arrested SE at a significantly lower dose (1mg/kg) than was effective in the absence of pentobarbital. Mean exposure of SAGE-547 was 180±61 nM in plasma and 212±83 nM in brain at 15 minutes following iv bolus.

Conclusions: SAGE-547 was able to arrest seizure activity in this model of pharmaco-resistant SE at plasma exposures comparable to those achieved in an ongoing clinical study of SAGE-547 in super refractory SE (SRSE). These results suggest that the lithium-pilocarpine model of pharmaco-resistant SE may be a useful translational bridge to assess the utility of novel neuroactive steroids for the treatment of status epilepticus.

P08

The influence of ketogenic diet on the elemental and biochemical composition of hippocampal formation

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A growing body of evidence demonstrates that dietary therapies, mainly ketogenic diet (KD), may be highly effective in the reduction of epileptic seizures. All of them share the common characteristic of restricting carbohydrate intake to shift predominant caloric source of the diet to fat. Catabolism of fats results in the production of ketone bodies which become alternate energy substrates to glucose. Although many mechanisms by which ketone bodies yield its anticonvulsant effect are proposed, the relationships between the brain metabolism of the ketone bodies and their neuroprotective or antiepileptogenic action still remain to be discerned. In the present study, X-ray fluorescence microscopy and FTIR microscopy were used to follow ketogenic diet-induced changes in the elemental and biochemical composition of rat hippocampal formation tissue. The use of synchrotron sources of X-rays and infrared allowed us to examine changes in the accumulation and distribution of selected elements and biomolecules (proteins, lipids, ketone bodies, etc.) with micrometer spatial resolution. The comparison of rats fed with ketogenic or standard laboratory diets showed significant differences in Se, Zn and Ca areal densities and KD-induced anomalies in Zn and Ca levels were similar to those which we previously observed for animals in the acute phase of pilocarpine-induced seizures. Biochemical analysis of tissues taken from KD fed rats showed an increased intensity of 1740 cm^{-1} absorption band what was probably the result of elevated accumulation of ketone bodies. Moreover, increased ratio of absorbance at 1635 and 1658 cm^{-1} in the dentate gyrus and elevated frequency of creatine deposits in the CA3 hippocampal sector were found for high fat diet treated animals.

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P09

Nicotine partially suppresses evoked cortical discharges in adolescent rats exposed to hypoxia

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Background: Nicotine is widely used drug of abuse and the main psychoactive ingredient of tobacco smoking. This study focused on the possible beneficial effects of nicotine against the high-altitude hypoxia (9000 m for one hour) on 35–day-old rats.

Methods: 15 min prior to hypoxia exposition rats were treated with nicotine. Next day electrodes have been implanted and the effects of nicotine and hypoxia (or both factors) on duration of afterdischarges (ADs) were tested.

Results: Administration of nicotine declined the hypoxia-induced mortality in 35-day-old animals, moreover brought about suppression of ADs in experimental animals. Taken together, our data show that nicotine exhibits an anticonvulsant effect in adolescent rats. The mechanisms of nicotine neuroprotective properties include probably the influence of calcium homeostasis, increase synthesis of variety of growth factors, inhibition of the caspase cascades and antioxidant capability of nicotine.

P10

Status epilepticus induction has prolonged effects on the efficacy of antiepileptic drugs in the 6 Hz seizure model

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Background: Several factors may influence the efficacy of antiepileptic drugs (AEDs) in patients with epilepsy and treatment resistance could be related to genetics, neuronal network alterations, modification of drug transporters or targets. Consequently, preclinical models used for the identification of potential new, more efficacious AEDs, should reflect at least few of these factors. Previous studies indicate that induction of status epilepticus (SE) may alter the efficacy of AEDs and that this effect could be long-lasting. In this context, we wanted to assess the protective effects of mechanistically diverse AEDs in mice subjected to pilocarpine-induced SE using another seizure model.

Methods: We first determined seizure thresholds in mice subjected to pilocarpine-induced SE in the 6 Hz model, 2 and 8 weeks following SE. We then evaluated the protective effects of mechanistically diverse AEDs in epileptic and control animals.

Results: No major differences in 6 Hz seizure susceptibility were observed between control groups, while the seizure threshold of pilocarpine mice at 8 weeks after SE was higher than at 2 weeks, and higher than in control groups. Treatment with AEDs revealed major differences in drug response depending on their mechanism of action. Diazepam produced a dose-dependent protection against 6 Hz seizures in control and pilocarpine mice, both at 2 and 8 weeks after SE, but with an increased potency in epileptic animals; this increase was more pronounced at 2 weeks. Levetiracetam induced a potent and dose-dependent protection in pilocarpine mice, 2 weeks after SE, while its protective effects were observed only at much higher doses in control mice. Its potency decreased in epileptic mice at 8 weeks and was very limited (30% protection at the highest tested dose) in the control group. Finally, carbamazepine induced a dose-dependent protection at 2 weeks in control mice, but only limited effect (50% at the highest tested dose) in pilocarpine mice. Its efficacy decreased in both groups at 8 weeks after SE.

Conclusions: These experiments confirm that prior SE may have an impact on both potency and efficacy of AEDs and indicate that this effect may be dependent on the underlying epileptogenic processes.

P11

Canine status epilepticus: response to fosphenytoin is similar to human status epilepticus

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Background: There are a number of drugs that in induced rodent models, show great potential for human status epilepticus (HSE), but the leap to human is great and an inter-

mediate species with naturally occurring epilepsy would be of significant help in determining safety, efficacy, and target dose/plasma concentration. This proof of principle study was done to determine if canine status epilepticus (CSE) could be a translational platform.

Methods: 4 research dogs were used to determine pharmacokinetics of intravenous fosphenytoin (FOS) and simulate doses to be used in a double-blind, placebo-controlled study of FOS in CSE for client owned dogs presenting to veterinary emergency centers. Total and unbound phenytoin (PHT) concentrations were also measured as part of the clinical trial.

Results: Based on the pharmacokinetic study, a 15 mg/kg PE FOS dose was predicted to attain unbound plasma PHT concentrations similar to those reported effective for human SE and was used for the clinical trial. 50 dogs with CSE in 4 veterinary centers were enrolled. All were treated initially with diazepam, and 31 had additional seizures qualifying them as benzodiazepine resistant. Of the 31 treated, 22 received FOS and 9 placebo. At 12 hours 63 % receiving FOS had no further seizures compared with only 22% receiving placebo (p=0.042). The unbound PHT concentrations at 30-60 minutes were within the therapeutic concentrations for people with the exception of one dog.

Conclusion: At unbound plasma PHT concentrations observed with FOS doses used in HSE, the FOS response in CSE was similar. This suggests that CSE is similar enough to HSE to be considered as a translational platform to screen drugs effective in rodent models for potential trials in HSE. Our trans-disciplinary group has ongoing and planned studies in dogs of novel IV and Intranasal drugs for SE and acute repetitive seizures.

P12

Ultrasound stimulation improves behavioral outcome in an experimental model of mesial temporal lobe epilepsy

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Background: Epilepsy is one of the most common neurological diseases. The current therapeutic methods of epilepsy mainly focused on pharmacological or invasive surgical management. Recently, ultrasound (US) stimulation is considered as a promising tool for noninvasive treatment of brain diseases including epilepsy. However, in temporal lobe epilepsy (TLE), a common form of epilepsy, neurophysiological and functional outcomes following US stimulation are not well defined. To address this, in this study, we developed a paradigm of transcranial pulsed US stimulation to efficiently suppress seizure activity in a kainate (KA)-induced mouse model of mesial TLE.

Methods and Results: A mesial TLE mouse model was generated with a unilateral injection of KA into hippocampal CA3 region. The pulsed US stimulation inhibited acute seizure activities and suppressed SE or delayed the onset of the SE. Strikingly, the number of spontaneous recurrent seizures (SRSs) was reduced in a chronic period of KA- and US-treated mice. In addition, the KA- and US-treated mice exhibited improved performance in behavioral tasks assessing anxiety, sociability, and depression.

Conclusions: Our results demonstrate that US stimulation lead to inhibition of SRSs and improves behavioral outcome in a mouse model of mesial TLE. The present study suggests that noninvasive transcranial pulsed US stimulation is feasible to be adjuvant therapy in patients with epilepsy.

P13

Electrical status epilepticus during slow sleep in children with various forms of epilepsy

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The annual incidence of convulsive Status epilepticus among children in developed countries is about 20 per 100,000 population. Status epilepticus remains an important subject, because of the significant morbidity and mortality that attends some types of SE. Such potential morbidity represents a medical emergency, and engenders the need for rapid and accurate diagnosis and for effective and safe treatments. This definition initially referred to clinically obvious or generalized convulsive status epilepticus (GCSE), the advent of continuous electroencephalographic (EEG) monitoring has facilitated the recognition of subtle convulsive and nonconvulsive (NCSE) forms of status epilepticus. The notion of electrical status epilepticus during slow sleep (ESES) is EEG pattern characterized by diffuse spike-waves occurring during at least 85% of slow sleep and persisting on 3 or more records over a period of at least 1 month.

The purpose of the study is to analyze the specific characteristics of seizures in children which had electric status epilepticus during sleep.

Materials and methods: 1600 EEGmonitoring was carried out for three years in neurophysiological laboratory of neurology department (inpatient and outpatient), EEG was performed for 3 hours and more. 690 (43%) children of them had not seizures, complained about the delay in development and different paroxysmal states. Other children (910-56%) had convulsions of different types. 560 (35%) children have been severe epilepsy.
Research data: The analysis of bioelectric activity in 75 (5%) of children in the EEG showed signs of ESES-electrical status epilepticus during sleep. Clinical examination of these children showed that almost all children have delayed development, seizures in history. 25 children had more frequent attacks at the time of the investigation, and 11 children not had seizure at the moment of examination. Most of the children had severe developmental delay. There is an interesting fact - girls 10 years old, who had only 2 tonic-clonic seizure in history, not had development and mental delay, a good student at school, but had ESES on EEG. On her EEG was found regional continuous epileptic activity.
Seizures in children had different type- regional and secondary generalized tonic-clonic seizures in 15% children, myoclonic seizures -8%, absences -3%, in the majority of children -74% recorded polymorphic atack- tonic spasms with tonic-clonic seizures, atypical absences with myoclonia, atonic seizures.

Children with ESES on EEG had the following diagnoses: syndrome pseudo-Lennox, Landau Kleffner syndrome, consequence of acute stroke, epilepsy with electrical status epilepticus during slow sleep, Lennox Gastaut syndrome.

P14

Intracortical electroencephalography and multimodal neuromonitoring in comatose patients with acute brain injury: report of 3 cases

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Background: Nonconvulsive seizures (NSzs) and nonconvulsive status epilepticus (NCSE) are relatively frequent in

comatose patients with acute brain injury (ABI). The use of conventional surface electroencephalography (EEG) for continuous monitoring has significant limitations in the intensive care unit (ICU) setting including poor signal-to-noise ratio, insensitivity to capture localized seizures and movement artifacts. Early experience with the use of depth electrodes suggest that many of the limitations of scalp EEG recordings can be overcome. We describe our preliminary experience with 3 patients with ABI in whom intracortical EEG (iEEG) and multimodal neuromonitoring was carried out.

Methods: Commercially available eight-contact Spencer minidepth electrodes (AD-Tech, Racine, WI) designed for clinical iEEG recording were chosen for use. Intracortical electrode location where possible, were placed next to the damage tissue. In addition, 21 needle electrodes attached with collodion placed according the International 10-20 System were included. EEG was recorded using a digital video-EEG monitoring system (XLTEK). Moreover, insertion of other monitoring devices including intracranial pressure monitor (ICP), brain tissue oxygen monitor and brain temperature sensor was performed. This protocol was approved by the local Ethics Committee.

Results: There were 2 men and 1 woman. The mean age was 53 years. The study included one patient with traumatic brain injury, one patient with hypertensive hematoma in the basal ganglia and one patient with subdural hematoma. All three patients had invasive monitoring devices placed bedside in the ICU. Continuous EEG monitoring lasted from 3 to 5 days. In one patient, iEEG was placed in the hemisphere contralateral to the lesion. None of the 3 patients had seizures. Asymmetry of the background activity, rhythmic delta waves and occasional focal epileptiform discharges were some of the most important neurophysiological findings. Conclusions: Invasive multimodal brain monitoring is a feasible technique that can be performed without complications in patients with severe ABI, and its use can shed light on the intrinsic pathophysiological mechanisms of NSzs and NCSE in comatose subjects.

P15

Epileptiform activity in patients treated with therapeutic hypothermia after cardiac arrest: Is it status?

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With the implementation of therapeutic hypothermia (TH) after cardiac arrest (CA) the neurocritical care community has been trying to redefine the value of the parameters previously used to predict neurologic outcome. The EEG during the TH or shortly after is an important asset for this porpoise, however, whether the usual patterns of epileptiform activity found in these patients reflect an ictal phenomenon or not remains controversial in many cases.

Methods: We retrospectively reviewed the electronic medical records of all patients undergoing TH after CA from January 2011 until December 2014. We identified the patients with any type of epileptiform activity and reviewed their EEGs.

Results: Sixty three patients were included. Forty six died. Epileptiform activity was found in 16 patients (25.4%), from whom only 2 had a favorable outcome (CPC 1 or 2). Twelve fulfilled Non Convulsive Status Epilepticus (NCSE) criteria, and 4 had patterns that fall into the "Ictal-Interictal Continuum"; repetitive and non-evolving generalized epileptiform discharges (GPDs) at a rate of 2-2.5 Hz, 2 over a suppressed background and 2 over a continuous, diffusely slow background.

When treating with benzodiazepine trials our patients with the 2-2.5 Hz GPDs over a suppressed background, even though they remained comatose, the epileptiform discharges stopped, and a continuous theta background appeared, two of them presenting background reactivity as well. Two of these patients died and the other one remains in a persistent vegetative state.

This finding suggest that the pattern of GPDs at 2-2.5 Hz over a suppressed background may represent an ictal pattern in this specific clinical context.
The 2 survivors developed the Status at day 4/5 post CA, after weaning Midazolam in the normothermia phase, and in both the EEG background was reactive in the previous days and also after the benzodiazepine trial. These specific circumstances were not present in any of the other patients with epileptiform activity.

Conclusions: Epileptiform activity is common in comatose patients treated with TH after CA. The presence of epileptiform activity during TH Is associated with poor outcome. The SE developed after Midazolam stoppage and with previously reactive EEGs should be treated aggressively.

P16

Prediction of rhythmic and periodic EEG patterns and seizures on continuous EEG with early epileptiform discharges

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Background: Nonconvulsive seizures (NCS) and nonconvulsive status epilepticus (NCSE) as well as rhythmic and periodic EEG patterns of 'ictal-interictal uncertainty' (including periodic discharges, rhythmic delta activity and spike-and-wave complexes) frequently occur in neurological intensive care patients. EEG is obligatory but the diagnosis remains difficult. Most authors recommend the use of continuous EEG (cEEG) but large amounts of data are produced. Furthermore recent studies showed lack of seizures in cEEG recordings if early epileptiform discharges were absent.

Objective: To assess the incidence and features of ictal EEG patterns and rhythmic or periodic EEG patterns of 'ictal-interictal uncertainty' in a prospective neurological critical care patient cohort with and without early epileptiform discharges.

Methods: Separate analysis of the first 30 minutes and the remaining segments of prospective cEEG recordings according to the ACNS Standardized Critical Care EEG Terminology (2012 version) as well as NCS criteria[1] and review of clinical data of 32 neurological critical care patients. All patients were referred to the 1st and 2nd Neurological Department, Hospital Hietzing, Vienna, because of suspected NCSE between July 2012 and July 2014. Results are visualized with NeuroTrend.

Results: A total of 17 patients suffered from epileptiform discharges in the first 30 minutes. In the remaining cEEG recording segments 23.5% (n=4) of these patients had electrographic seizures, 64.7% (n=11) showed rhythmic or periodic EEG patterns of 'ictal-interictal uncertainty' and 11.8% (n=2) had no rhythmic or periodic EEG patterns. No electrographic seizures were recorded in patients without early epileptiform discharges. 26.7% (n=4) showed rhythmic or periodic EEG patterns of 'ictal-interictal uncertainty' and 73.3% (n=11) had no rhythmic or periodic EEG patterns in the remaining cEEG recording. These findings were statistical significant (p=0.008).

Conclusions: In the present study rhythmic and periodic EEG patterns of 'ictal-interictal uncertainty' occurred more frequently than electrographic seizures in neurological critical care patients. Both EEG findings were significantly more frequent in patients with early epileptiform discharges.

[1] Chong DJ & Hirsch LJ. Which EEG patterns warrant treatment in the critically ill? Reviewing the evidence for treatment of periodic epileptiform discharges and related patterns. J Clin Neurophysiol 22,79–91 (2005).

P17

NeuroTrend: prospective validation of rhythmic and periodic pattern detection in the ICU

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Background: NeuroTrend is a computational method that analyses long-term scalp EEGs in the ICU according to ACNS standardized critical care EEG terminology (CCET) including electrographic seizures. At present it attempts to become a screening aid for continuous EEG (cEEG) recordings in the ICU to facilitate the review process and optimize resources.

Methods: A prospective multi-center study was performed in two neuro-ICUs including 68 patients who were subjected to video cEEG. Two reviewers independently annotated the first minute of each hour in the cEEG according to CCET. These segments were also screened for electrographic seizures. The matching annotations (2911 segments) were then used as gold standard condition to test sensitivity and specificity of the rhythmic and periodic pattern detection of NeuroTrend.

Results: Interrater agreement showed substantial agreement for localisation (main term 1) and pattern type (main term 2) of the CCET. The overall detection sensitivity of NeuroTrend was 94 % with high detection rates for periodic discharges (PD = 82%) and rhythmic delta activity (RDA = 89%). Overall specificity was moderate (67%) mainly due to false positive detections of RDA in cases of general slowing. In contrast a detection specificity of 87% for PDs was reached. Localisation revealed only a slight agreement between reviewers and NeuroTrend.

Conclusions: NeuroTrend is a suitable screening tool for cEEG in the ICU and will raise the efficiency of long-term EEG monitoring in the ICU. At this stage, pattern localisation and differentiation between RDA and general slowing needs improvement.

P18

Ictal and Interictal EEG patterns in patients with non-convulsive and subtle-convulsive status epilepticus

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Background: EEG findings in non-convulsive or subtle-convulsive status epilepticus (NCSE and SCSE respectively) can be heterogenous. We aim to study the different patterns on EEG in our cohort of patients.

Objective: To study ictal and interictal EEG patterns in patients with NCSE and SCSE.

Methods: From January 2012 to December 2013, EEGs recorded from patients admitted for altered mental status suspected of having NCSE or SCSE were reviewed retrospectively. EEG Status was defined as having (a) continuous ictal discharges lasting >5 min or (b) >2 discrete bursts of ictal discharges, each lasting <5 min, without returning to previous background rhythm in between these bursts.

Results: Among 1698 EEGs recorded for at least 30 minutes from hospitalized patients, 55(3.23%) satisfied the criteria of EEG SE.
The ictal onset was regional in 37 (67.2%) EEGs, multiregional independent in 8 (14.5%) and generalised in 10 (18.4%).
The EEG seizure duration was >5 min in 24 (43.6%) EEGs, between 1 to 5 min in 14 (25.4%), and less than 1 min in 17 (30.8%).
20 (36.3%) EEGs showed one continuous prolonged seizure episode of >5 min duration, 15 (27.2%) had 10 or less discrete episodes, 20 (36.3%) had more than 10 episodes, and 11 (20%) had 2 or more ictal patterns.
30 (54.5%) EEGs had onset ictal frequency of $\geq$ 8 whereas rest had < 8 Hz ictal frequency.
In the inter-ictal segment, 29 patients had continuous generalised slow waves, while 12 had intermittent generalised slow waves. 11 patients had continuous slow waves lateralised to one hemisphere and these were ipislateral to the ictal focus in 10 but contralateral in 1. Other interictal waves seen were PLEDS (6), sharp waves (3), suppression (5), and triphasic waves (1).
The background alpha rhythm was absent in 36 patients, slow in 14 and normal background alpha was seen in inter-ictal period in 5 patients.

Conclusion: The ictal and interictal EEG in NCSE and SCSE can be varied. Further study to look for etiologic and clinical correlates of each pattern could add to its clinical value.

P19

New-onset refractory status epilepticus: etiology, clinical features and outcome

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Background: New-onset refractory status epilepticus (NORSE) is a recently described entity characterized by the occurrence in young and healthy adults of a long period of refractory seizures without obvious explanation. The aims of this study were to determine the etiology and describe the clinical features of NORSE, including therapeutic approaches, and explore determinants of outcome.

Methods: Retrospective review of patients with de novo RSE without clear etiology identified within 48h of admission between January, 1 2008 and December, 31 2013 in 13 medical centers of the Critical Care EEG Monitoring Research Consortium (CCEMRC). The primary outcome measure was mortality at discharge.

Results: Of 130 cases, 67 (52%) remained cryptogenic. The most common identified etiologies were autoimmune (25 [19%]) and paraneoplastic (23 [18%]) encephalitis. Full data were available in 125 cases (62 cryptogenic). Poor outcome was seen in 77/125 (62%) cases, and 28 (22%) died. Predictors of mortality included older age, duration of SE, anesthetics, and complications. Among the 63 patients with available follow-up data (median 9 months), functional status improved in 36 (57%) and 79% had good or fair outcome at last follow-up but epilepsy developed in most (92%). Immune therapies were used less frequently in cryptogenic cases, despite a comparable prevalence of inflammatory CSF changes.

Conclusions: Autoimmune encephalitis is the most commonly identified cause of NORSE, but half of cases have no clear etiology. Outcome at discharge is poor but improves during follow-up. Epilepsy develops in most cases. The role of anesthetics and immune therapies warrants further investigation.

P20

Incidence of recurrent seizures in patients with LPDs (PLEDs) and non-convulsive seizures recorded on continuous EEG in the critical care setting

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Background: The use of continuous EEG (cEEG) monitoring has revealed patients with epileptiform discharges and/or seizures after acute primary brain injury. The majority of the seizures are without clinical signs and were historically overlooked. Continuous EEG in the ICU has helped to identify the seizures, but understanding the implications of these epileptiform discharges (LPDs) and EEG seizures are more complex. The aim of this study is to investigate the incidence of recurrent seizures and their predictors in patients with LPDs and non-convulsive seizures(NCS) in patients in the critical care setting.

Methods: We screened 1163 patients who had cEEG during 2013 and 200 consecutive patients with LPDs and/or NCS seizures were examined using our EEG reporting database. Patients with less than 3 months of out-patient follow up were excluded from analysis. Remaining patients were divided into three groups: LPDs + NCS/NCSE (A), LPDs only (B), NCS/NCSE only(C). Their demographic details, etiology of acute presentation, previous history of epilepsy, recurrent seizure and anti-epileptic drug (AED) history was extracted from chart review.

Results: 118 patients, after review of patient records, qualified for the study. Group A, B, C had 51, 45 and 22 patients respectively. The three groups were well matched by age, gender and history of epilepsy. Most common etiology was hemorrhage, tumors and unknown in group A, B, C respectively. 54.1% patients with LPDs (Group A and B) had focal lesion compared to 22.7% in group C ($p<0.01$). Only 24.4% in LPDs only group developed epilepsy compared to 60.7% and 90.9% patients in Group A and C ($p<0.01$). 77.7% of patients in group B were on AEDs compared to more than 90% in the other groups.

Conclusion: Patients with non-convulsive seizures in the ICU were very likely to develop recurrent seizures after discharge from the ICU with 90% of the patients with NCS alone, less with NCS plus LPDs (60%) while patients with LPDs were more likely to have a focal pathology and had the lowest incidence (24%) of recurrent seizures. Prospective studies are required to learn more about the long term implications of LPDs and non-convulsive seizures in ICU patients.

P21

Dynamics and variability of burst suppression in pharmcological coma for refractory status epilepticus

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Evidence to support the efficacy of pharmacologically induced coma targeting electroencephalogram (EEG) burst suppression in treating refractory status epilepticus (RSE) has been limited. A prominent retrospective study for instance concluded that burst suppression failed to impact patient outcome, and several recent papers have provided evidence for net harm. These findings contrast starkly with the theoretical argument that a state of profound brain inactivation as marked by burst suppression should be neuroprotective. We sought to understand this mismatch of expectation and outcome by analyzing EEG recordings from 8 patients with RSE treated with propofol and/or midazolam. 2 of the 8 patients had a period of cardiac arrest before the onset of RSE (post-anoxic RSE, pRSE). We used a previously validated algorithm to detect suppressions, and quantified the depth of burst suppression vs time using the burst suppression probability (BSP) - a continuous measure ranging from 0 (absence of burst suppression) to 1 (fully suppressed / isoelectricity). We compared the resulting BSP to a clinically specified target level of 0.8+/-0.15. We found that patients remained in the target range for 0-79.7% (average=22.2%, SD=31.3%) of the total time under treatment. The average time spend below and above the target range was 83.8% (SD=32.8%) and 0.5% (SD=1.3%) respectively for non-post anoxic patients (npRSE); 43% and 14% for pRSE patient. The proportion of time during which an individual patient successfully achieved at least small degree of burst suppression (BSP > 0.05) varied substantially, with an average=65.1% (SD=26.9%). The average deviation of BSP from target level was -0.45 (SD=0.28) and can fluctuate as much as 200% within individuals over time. These results show that burst suppression achieved in clinical practice is heterogeneous and highly variable. Despite the intensive efforts involved, including regular EEG monitoring and adjustment by experienced clinical team, we are unable to maintain patients within the prescribed therapeutic limits. This significant variability in the dynamics and depth of pharmacological coma may be the reason that theoretical benefits of burst suppression for RSE are not realized in practice, and points to the need for an alternative paradigm for managing burst suppression targeting-pharmacological coma.

P22

Yield of continuous EEG using the 2012 ACNS terminology in outcome prediction after status epilepticus

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Background: Continuous electroencephalography (cEEG) has an important role for seizure detection and treatment guidance [1] and is recommended for SE management [2]. The role of cEEG in outcome prediction is less clearly defined [3], and with inconsistent findings [4, 5].

Methods: cEEG data of 120 consecutive adults patients with SE were collected prospectively in three tertiary medical centers using the 2012 American Clinical Neurophysiology Society's Standardized Critical Care EEG Terminology. Association between cEEG features and two clinical outcome measures (mortality and complete recovery) was assessed.

Results: In the first 24 hours of EEG recording, 49 patients (40.8%) showed no periodic or rhythmic pattern, 45 (37.5%) had periodic discharges, 20 (16.7%) had rhythmic delta activity, and 6 (5%) had spike-and-wave discharges. 68.3% of patients had seizures during the record. After adjusting for known clinical predictive factors for mortality including the Status Epilepticus Severity Score (STESS) and the etiology, the only EEG features (among rhythmic and periodic patterns, seizures, and background activity), that remained significantly associated with outcome were the absence of a posterior dominant rhythm (OR: 9.8; $p = 0.033$) for mortality and changes in stage II sleep pattern characteristics (OR: 2.59 for each step up among these categories: absent, present and abnormal, normal; $p = 0.002$) for complete recovery.

Conclusions: This is the first report of the predictive value of cEEG monitoring for outcome prediction in SE since the publication of the 2012 ACNS report on Standardized Critical Care EEG Terminology. When adjusted for clinical predictors, EEG background feature gives independent information on outcome prediction as opposed to rhythmic and periodic patterns or seizure characteristics.

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P23

Extreme delta brush, could be an ictal pattern in patients with anti-NMDA receptor encephalitis

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Background: Anti-NMDA receptor (NMDAr) encephalitis associated syndrome includes neuropsychiatric symptoms, impaired consciousness, seizures, autonomic instability, and hypoventilation. The electroencephalographic (EEG) activity throughout the course of the disease has not been documented enough. We reviewed electroclinical data of patients with NMDAr encephalitis contributing to characterize their EEG and its clinical correlation.

Methods: We retrospectively identified 16 patients with NMDAr encephalitis. 15 of them underwent video-EEG in the acute phase in 8 Spanish Medical centres. The other was excluded because video EEG was performed outside the acute phase.

Results: 15 patients (11 females). Median age 37.4 (range 14-87) years. Seizures occurred in 9 (6o%), and status epilepticus (SE) in 5 (33,3%;), MRI was abnormal in 10 (66.6%), and CSF was normal in 3 and abnormal in 12 with positive PCR for mycoplasma pneumoniae (1/15) and virus herpes simple (1/15). Ovarian teratoma was found in 1 patient, other malignacies (small cell lung carcinoma) in 1 patient. EEG was abnormal in acute phase in 14/15 (93.3%). Extreme delta brush (EDB) was observed in 5 (33.3%), the presence of EDB was associated with SE in all cases (3 subtle SE and 2 non convulsive SE). Rhythmic delta activity without EDB 5 (33.3%). Excessive beta was present in 4 (26.6%).

Conclusions: Almost invariably, patients with NMDAr encephalitis had abnormal EEG. The presence of EDB is associated with seizures and SE in our patients. This results suggest that EDB EEG finding constitutes an ictal EEG pattern.

P24

Forehead EEG electrode compared to full-head scalp EEG in 100 patients with altered mental state

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Background: We have recently introduced a forehead EEG electrode set (Myllymaa et al., J Neurosci Methods, 2013:30;103-9) that is suitable for e.g., emergency EEG in patients with altered mental state. Using this set, first clinical experiences in 13 patients with clinical Status Epilepticus (SE) suspicion are encouraging (Lepola et al., J Clin Monit Comput, 2015, DOI 10.1007/s10877-014-9652-9).

Methods: 100 consecutive acute neurological patients (53 women, 47 men, age 18-90 years) with unexplained altered mental state were studied with acute emergency EEG to rule out SE. EEGs were recorded simultaneously with forehead EEG electrode and routine 10-20 system full-head scalp electrodes to compare usability of forehead EEG electrode in this setting. EEGs were interpreted blindly first only based on forehead EEG, and then by full-head EEG. 100 EEGs were interpreted by two experienced clinical neurophysiologists. Inter-rater agreement was also assessed.

Results: 96/100 of the patients did not show EEG evidence of SE. There was 100 % agreement with forehead and routine EEG. 4/100 showed EEG evidence of SE in routine EEG, with 50% agreement between different electrode types. Two SEs were not seen in forehead EEG.These false-negative forehead EEGs included one posterior partial SE and one where EEG was obscured with abundant patient-related artifacts. Inter-rater agreement on reading forehead EEG was high (100% with true negative and true positive EEG findings).

Conclusions: Acute forehead EEG electrode showed 100% agreement with conventional full-head scalp-EEG when no evidence of SE was seen, without false-positive findings. In 4 cases with SE, the forehead EEG showed 50% agreement with full-head EEG. Two false-negative cases were explained by localized posterior SE beyond the forehead electrode and with patient-related artifacts. The forehead electrode is suitable for acute EEG recordings.

P25

Thai national data of status epilepticus: 9 years

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Background: Status epilepticus (SE) is a major neurological emergency that is associated with a significant mortality. The national database of SE in Thailand and other developing countries is limited in terms of characterize the demographics, outcome and prognostic factor.

Methods: We retrospectively explored national data in Thailand for reimbursement of all adult SE patients admitted in the fiscal year 2004-2012. SE patients were diagnosed and searched based on ICD 10 (G41) from the national database with Universal Health Coverage Insurance.

Results: We found 12,367 SE patients. The average age was 48.14 years (18-104 years) and 8,119 patients were males (65.7%). Discharge status of most SE patients was improved (9,231 cases, 74.6%), while 2,033 patients (16.4%) did not improved.In-hospital mortality was 8.4% (1,045 of 12,367 patients). Only 58 patients (0.5%) showed complete recovery. The most common comorbidities diseases were hypertension (1,790 patients, 14.5%); DM (1,064 patients, 8.6%) and previous stroke (819 patients, 6.6%).Respiratory failure was the most common complication in 3,990 patients (32.3%). Hospital length of stay was (mean [SD]) 5.48 (11.44) days. Age, sex, hospital level, region and comorbidities such as previous Stroke, HT, CNS infection, Cirrhosis and respiratory failure were associated with poor functional outcome ($p<0.001$)

Conclusion: This finding will be crucial for developing management of SE in Thailand. Provides educational pro-

grams is necessary for reduce hospitalized rate and early employment of intensive care procedures should be considered. The effective management of SE in the emergency department may help to prevent of death caused by SE.

P26

A retrospective analysis of 23 cases of non-convulsive status epilepticus in an acute care hospital in Japan

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Background: Non-convulsive status epilepticus (NCSE) is an emerging neurological condition that is still underdiagnosed or misdiagnosed in Japan. The aim of this study was to evaluate the clinical manifestation, electroencephalographic (EEG) patterns and outcome of NCSE in an acute care hospital in Japan.

Methods: We retrospectively analysed 23 patients with NCSE who had been admitted to our hospital between April 2011 and November 2014. EEG patterns were classified using the EEG criteria for NCSE proposed by Sutter and Kaplan in 2012.

Results: There were 9 males and 14 females with a mean age of 68.7 years (range, 30-95 years). The underlying disorders were diverse (dementia 3, Hashimoto encephalopathy 2, traumatic brain injury 2, cardioembolic infarction 1, subarachnoid hemorrhage 1, herpes simplex encephalitis 1, non-herpetic acute limbic encephalitis (NHALE) 1, Creutzfeldt-Jakob disease 1, hypoplasia of the corpus callosum 1, hydroencephalodysplasia 1, schizophrenia 1, systemic lupus erythematosus 1, liver cirrhosis 1, chronic renal failure 1, idiopathic thrombocytopenic purpura 1, leukemia 1, theophylline intoxication 1, not specific 2). The EEG patterns were also diverse (complex partial status epilepticus 10, NCSE in the postictal phase of tonic-clonic status epilepticus 7, aura continua 2, typical absence status epilepticus 2, de novo absence epileptiform EEG changes 1, drug-induced confusional state with epileptiform EEG changes 1). Only 5 patients had a history of epilepsy. The levels of antithyroid antibodies were elevated in the two patients with Hashimoto encephalopathy, and in one of them the level of autoantibody against the NH_2-terminal of alpha-enolase was also elevated. The level of anti-glutamate receptor ε2 antibody was elevated in the patient with NHALE. The outcomes of NCSE were good in patients whose underlying disorders had been sufficiently controlled.

Conclusions: NCSE should be diagnosed as early as possible using EEG in order to avoid underdiagnosis.

P27

Seizures and status epilepticus in air medevac patients

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Background: Many patients with prolonged seizures or status epilepticus are transported to our hospital via helicopter, often from regional emergency departments. In patients with status epilepticus, early treatment intervention has been shown to be critical and the pre-transport, transport, and post-arrival diagnostic and therapeutic management may affect outcome. In addition, we hypothesized that in some cases conditions that mimic prolonged epileptic seizures were undergoing potentially unnecessary treatment and transport.

Methods: We performed a retrospective chart review of all adult patients transported by Vanderbilt LifeFlight to our medical center from October, 2006 through April, 2014 with a transport diagnosis of seizures or status epilepticus and identified 104 cases. We assessed the discharge diagnosis, diagnostic value of EEG and neurological outcome in this population.

Results: The most common discharge diagnosis of air medevac transferred patients was new onset seizures (45 patients) followed by breakthrough seizures (37 patients), psychogenic non-epileptic seizures (PNES) (18 patients), and syncope (4 patients). EEG was performed within 24 hours in 62 patients (60%) and was considered diagnostic in 32% of these cases. Sixty-one percent of patients (62/104) were intubated prior to arrival including 44% (8/18) of patients found to have PNES. At discharge, 76% (79/104) of patients were at neurological baseline, 20% had a neurological deficit and 3 patients died in hospital.

Conclusions: The population undergoing air medevac for seizures is heterogeneous with new onset seizures and breakthrough seizures nearly equally represented. PNES makes up a substantial subset of these patients and represents a population of patients who potentially underwent unnecessary treatment and transfer. Future work will evaluate whether treatment influences outcome and to establish protocols for management of these patients.

P28

The syndrome of typical absence status epilepsy at elderly

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Background: the absence status epilepticus is a prolonged, generalized absence seizure that usually lasts for hours and can even last for days.

Methods: a case report of de novo absence status epilepticus. A 69-year-old woman was brought to our emergency room due to altered mental status and speech disturbance. She was no epilepsy in anamnesis and family history. MRI: no acute lesions. EEG monitoring demonstrated continuous generalized spike wave or polyspike wave activity (2-4Hz). Successful treatment by intravenous administration of Valproate and Levetiracetam (15mg/kg).

Conclusion: Syndrome of typical absence status epilepsy at elderly often remains not distinguished, detailed anamnesis and continuous EEG monitoring are necessary to avoid misdiagnosis and inadequate treatment.

P29

De novo status epilepticus with isolated aphasia

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Background: Sudden onset of aphasia is usually due to stroke. Rapid diagnostic workup is necessary if reperfusion therapy is considered. Ictal aphasia is a rare condition but has to be excluded. Perfusion imaging may differentiate acute ischemia from other causes. In dubious cases EEG is required but time consuming and laborious.

Methods: Case report of de novo status epilepticus with aphasia and review of the literature.

Results: A 62 year old right handed women presented to the emergency department after nurses found her aphasic. She had undergone operative treatment of varicosis 3 days ago. Apart from hypertension and obesity no cardiovascular risk factors and no intake of medication other than paracetamol were reported. Neurological examination revealed global aphasia and right pronation in the upper extremity positon test. CT with angiography and perfusion showed no abnormalities. EEG performed after the CT scan showed left sided slowing with high voltage 2/s Delta waves but no clear ictal pattern. Intravenous lorazepame did not improve EEG or aphasia. Lumbar puncture was performed which excluded encephalitis. MRI showed cortical

pathological diffusion imaging and cortical hyperperfusion in the left parietal region. Intravenous anticonvulsive therapy under continuous EEG resolved neurological symptoms. The patient was kept on anticonvulsive therapy. MRI control after 6 months showed no abnormalities along with no clinical abnormalities.

Conclusions: Status epilepticus can mimic stroke symptoms and has to be considered in patients with aphasia even when no previous stroke or structural lesions are detectable and EEG shows no epileptic discharges. Epileptic origin is favoured when CT or MR imaging reveal no hypoperfusion. In this case MRI was superior to CT to detect hyperperfusion.

P30

Febrile illness-related epilepsy syndrome (FIRES): A compilation of 6 patients and literature review

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Febrile illness-related epilepsy syndrome (FIRES) is a catastrophic epileptic encephalopathy with poor outcomes. Despite remarkable stereotypical characteristics, it is without a known underlying etiology and is notoriously difficult to treat. Reports of this entity have increased exponentially over the past decade and the literature refers to FIRES with different names, making a comprehensive understanding of the disease challenging. Over 10 years, Seattle Children's Hospital has managed 6 cases of FIRES. The article serves to review those cases and offer a discussion on the current literature and knowledge of this disease in the hope of initiating a dialogue regarding more effective treatment and management for this devastating epileptic encephalopathy.

P31

Non-intravenous midazolam versus intravenous or rectal diazepam for the treatment of early status epilepticus: a systematic review with meta-analysis

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Background: Prompt treatment of status epilepticus (SE) is associated with better outcomes. Diazepam (DZP) and midazolam (MDZ) are commonly used in the treatment of early SE. Aim of this systematic review was to determine if non-intravenous (non-IV) MDZ is as effective and safe as intravenous or rectal DZP in terminating early SE seizures in children and adults.

Methods: We searched Cochrane Central Register of Controlled Trials (CENTRAL), ClinicalTrials.gov, and MEDLINE for randomised controlled trials comparing non-IV MDZ with DZP (by any route) in patients (all ages) with early SE, defined either as seizures lasting >5 min or as seizures at arrival in the emergency department. Following outcomes were assessed: clinical seizure cessation within 15 min of drug administration; serious adverse effects; time interval to drug administration; time from arrival in the emergency department to seizure cessation. Outcomes were assessed using a random-effects Mantel-Haenszel meta-analysis to calculate risk ratio (RR) and mean difference with 95% confidence intervals (95% CIs).

Results: Nineteen studies with 1933 seizures in 1602 patients (some trials included patients with more than one seizure) were included. 1573 patients were younger than 16 years. For seizure cessation, non-IV MDZ was as effective as DZP (any route) (RR: 1.03; 95% CIs: 0.98 to 1.08). No difference in adverse effects was found between non-IM MDZ and DZP by any route (RR: 0.87; 95% CIs: 0.50 to 1.50). Buccal MDZ was more effective than rectal DZP in terminating SE (RR: 1.78; 95% CIs: 1.11 to 2.85). Time interval between arrival and seizure cessation was significantly shorter with non-IV MDZ by any route than with DZP by any route (mean difference: -3.67 minutes; 95% CIs -5.98 to -1.36); a similar result was found for time from arrival to drug administration (mean difference: -3.56 minutes; 95% CIs -5.00 to -2.11).

Conclusions: Non-IV MDZ is as effective and safe as intravenous or rectal DZP in terminating early SE in children. Times from arrival in the emergency department to drug administration and to seizure cessation are shorter with non-IV MDZ than with intravenous or rectal DZP, but this does not necessarily result in higher seizure control.

P32

Duration of complex focal, secondary, generalised tonic clonic, and primary generalised tonic clonic seizures - a video EEG analysis

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Identifying seizures with prolonged duration (SD) during video-EEG monitoring is of importance to inform clinicians when to start emergency treatment of seizures to prevent status epilepticus. The aim of this study was to assess the clinical and electroencephalographic (EEG) SD in consecutive patients with epilepsy who underwent prolonged video-EEG monitoring and to identify a seizure type-dependent time-point to start emergency treatment, based on the likelihood that seizures do not stop spontaneously. Furthermore, we seek to determine predictors of SD and explore the relationship between antiepileptic drug (AED) serum levels and SD. Therefore, we retrospectively analysed 1796 seizures in 200 patients undergoing video-EEG monitoring between January 2006 and March 2008.

Focal simple seizures lasted significantly shorter (clinical SD 28 s, EEG SD 42 s) than focal complex seizures (clinical SD 64 s, EEG SD 62 s), and both seizure types lasted significantly shorter than secondarily generalised tonic-clonic seizures (GTCSs; clinical SD 90 s, EEG SD 96 s). There was no difference between duration of the convulsive phase of primarily (defined as non-focal) GTCSs and secondarily GTCSs (each 65 s). Cumulative clinical SD (99%) was seven minutes in focal complex seizures and 11 minutes in focal simple seizures. Mixed linear regression model demonstrated, that history of status epilepticus (P=0.034), lobe of seizure onset (P=0.040), and MRI lesions (P=0.013) were significantly associated with logarithmic EEG SD in focal epilepsies recorded with scalp electrodes. We found significant negative correlations between the AED blood level and EEG SD in patients treated with monotherapy: carbamazepine (P<0.001), levetiracetam (P=0.001), oxcarbazepine (P=0.001) and valproic acid (P=0.038), whereas no significant correlation coefficient was obtained between blood level of lamotrigine monotherapy and EEG SD.

Based on the results of this study, we propose 2 minutes of convulsive seizure activity (irrespective of focal or generalised onset) as time-based decision to start with treatment, which might serve as a working definition of convulsive status epilepticus. In focal complex seizures, we recommend to start with intravenous treatment after 7 minutes, in focal simple seizures after 11 minutes of ongoing seizure activity, and suggest those time-limits as clinically based definitions of impending status epilepticus in these seizure types. History of status epilepticus, temporal seizure onset and lesional MRI findings are factors associated with significantly longer SD. Negative correlations of carbamazepine, levetiracetam, oxcarbazepine and valproic acid serum levels and SD suggest a prolonging effect on seizures after withdrawal of these AEDs during Video-EEG monitoring sessions.

P33

Clinical patterns of status epilepticus in Egyptian children with tuberous sclerosis complex

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Background: Refractory epilepsy is a common clinical manifestation in patients with tuberous sclerosis complex (TSC), which could be complicated by many life-threatening conditions as status epilepticus (SE). Few reports mentioned the incidence, patterns and semiology of SE in those patients.

Objectives: To study the aetiology, clinical profile, and outcome of SE **in** TSC patients.

Methods: A cross sectional study was carried out on 36 Egyptian children with TSC, diagnosed according to the criteria of National Institutes of Health consensus conference, revised the diagnostic criteria for TSC addressing the history of SE and its clinical patterns in such patients. Clinical history, general and neurological examination and psychometric evaluation along with standard questionnaire were used to explore characteristics of epileptic manifestations of those patients. All included patients had their long term video EEG and MRI brain during or shortly after the SE episodes.

Results: Twenty one patients (58.3%) experienced SE along the disease duration (7.5 years ± 3.5), most of those patients had convulsive status epilepticus (CSE), and a minority had a non convulsive status epilepticus (NCSE), in addition to a number of patients who experienced serial fits exhibiting variable semiologies. The clinical criteria of those patients encompassed a history of infantile spasms (IS) in 14 patients (66.6%), severe mental retardation (MR) in 14 (66.6%), autistic behavior in 9 (42.8%), and severe epileptogenic EEG findings in 12 patients (57.1%). All of them had high tubers number (> 8), 5 patients (23.8%) had subependymal giant cell astrocytomas (SEGAs), of those, 2 patients developed de novo SEGAs by the time of experiencing their SE. Interestingly, 2 patients had their SE after receiving everolimus.

Conclusions: Incidence of SE in this sample is high (> 50%). Severe MR, autistic features, history of IS, high tubers burden seem to increase the risk for developing SE in patients with TSC.

P34

Evolution of MRI Features in Cerebral Parenchyma from Prolonged Focal Status Epilepticus: A Case Study

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It has rarely been documented that permanent alteration of cerebral structures occurs by a focal status epilepticus (FSE). We report a case of 16 year-old boy with a FSE in whom serial T1-weighted MR volumetry as well as conventional MRI was useful for investigating an evolving pattern of morphological changes that resulted during and after the FSE; cortical laminar necrosis (CLN), increased T2 signal intensities and marked regional atrophy on the corresponding areas. Despite the cessation of FSE after adequate medication (combination therapy including clobazam - 1mg/kg/day), further significant cerebral atrophy was detected at the limited regions where discrete CLN had occurred during the FSE.

P35

Progranulin in cerebro spinal fluid as a marker for cortical regeneration in status epilepticus

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Recently a mouse model showed that Progranulin, as a marker for neuroinflammation and as a neuronal growth factor, was elevated in mice hippocampus after Status Epilepticus. This elevated level might mirror compensating neuronal mechanisms after a devastating storm such as a Status Epilepticus.

Here we performed a retrospective analysis of Progranulin levels in Serum and Cerebro Spinal Fluid (CSF) in our patients (n=21), who underwent lumbar puncture as part of diagnostical work up after Status Epilepticus. We also measured CSF-Progranulin levels in patients after one single grand-mal seizure as a control group. Patients with an CNS-infection as underlying cause were excluded.

Results: In our cohort Progranulin levels in CSF and serum were not significantly elevated compared to our control group. Furthermore there was no correlation between Progranulin levels and the time window between lumbar puncture and Status Epilepticus, as it was seen in mice. Additionally even in cases of higher CSF Progranulin levels we found no impact on the clinical outcome after Status Epilepticus.

Conclusion: Although our cohort is very heterogeneous we conclude that Progranulin in Serum and CSF does not seem to be a suitable marker for neuronal recovery after Status Epilepticus in humans.

P36

Malignant migrating partial seizures in infancy (Coppola-Dulac syndrome) – 25 Russian cases

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Introduction: (MMPSI) are rare epilepsy syndrome with debut at the first 6 months of life and characterized by multiple continuous electroencephalographic and electroclinical focal ictal patterns involved different independent areas of both hemispheres with severe arrest of psychomotor development. Publication of the first case was done by G.Coppola et al. (1995) and the most cases (n=20) were observed and described by O.Dulac (2005).

Methods: At the period of 2006-2014 were newly revealed and investigated 13 children with malignant migrating partial seizures in infancy (MMPSI) of cryptogenic origin (7 boys and 6 girls) and 12 children with symptomatic cases (5 boys and 7 girls). For all the children were provided dynamic video-EEG monitoring, MRI and genetic tests.

Results: Family history of epilepsy in all patients was not burdened. No SCN1A and POLG mutations were found. In symptomatic analogs of MMPSI only two infants had cerebral dysgenesis: lissencephaly-pachygyria in one girl and polymicrogyria in another girl. One boy had rhizomelic chondrodysplasia punctata, type 2 (MIM 222765). Other 9 children had perinatal hypoxic-ischemic CNS disturbances. Follow-up of patients allowed to distinguish following subpopulations: 1) "Classical" form in the form of marked SE of migrating multifocal seizures, it is pharmacoresistant with a poor prognosis for psycho-motor development, seizures and life (12 cases); 2) Mixed-form (MMPSI + EME) with a combination of electro-clinical MMPSI characteristics, but also with the presence of fragmented "erratic" myoclonus and suppression-burst pattern with polyspike-wave discharges on EEG (5 cases); 3) "Moderate" form

with possible decrease in frequency of seizures during combined antiepileptic therapy (6 cases); 4) "subtle" form with only "subtle" minimal motor seizures, inhibitory seizures, multiple ictal patterns during sleep, leading to awakening (2 cases).

Conclusions: MMPSI is new form of epileptic encephalopathy and a special form of status epileptic in infancy. This type of severe epileptic encephalopathy could be divided on subtypes with specifications in clinical course, EEG-features and prognosis.

P37

Refractory status epilepticus due to SMART syndrome

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Background: Stroke-like migraine attacks after radiation therapy (SMART) is a late-onset complication of brain irradiation which pathophysiology is unknown. Most of patients have reversible neurologic symptoms and radiological findings.
The purpose is to present three patients with SMART syndrome who had clinical and neuroimage suggestive of status epilepticus.

Patients: Patient 1. 69-years-old woman who was treated with radiation therapy 14 years previously for right occipital metastases (breast cancer). She presented several episodes of headache, speech disturbances, weakness of left limbs with altered awareness.
Patient 2. 49-years-old man who was diagnosed of acute lymphatic leukemia and was treated with whole brain radiation 20 years before the onset of symptoms. He developed some episodes consisting of headache, numbness of right face and right arm and the latest episodes accompanied by visual disturbances followed by generalized tonic clonic seizures.
Patient 3. 40-years-old man who received cerebral irradiation after surgery of cerebellar medulloblastoma 20 years before. He suffered three episodes of behavioral disturbance, aphasia, headache, visual aura followed by left homonymous hemianopia.

Results: All of patients suffered seizures mostly with visual aura. EEG showed interictal epileptiform discharges or focal slowing. Brain magnetic resonance image (MRI), positrón emission tomography (PET) or ictal-single-photon emission computed tomography (SPECT) showed focal cortical hyperperfusion. On MRI focal diffusion restriction and focal Gadolinium-enhancement was observed. All patients were treated with antiepileptic drugs being effective in one of them. One patient needed anesthesic coma and the other patient responded to corticotherapy.

Conclusions: Taking into account clinical evolution and ictal neuroimaging studies, status epilepticus could explain the origin of these episodes in SMART syndrome. Although most of patients have reversible symptoms, in some cases aggressive treatment to avoid sequelae is needed.

P38

Inflammatory causes of status epilepticus

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Background: Status epilepticus (SE) etiologies are multiple and influence morbidity and mortality. Neuro-inflammatory causes of epilepsy are being increasingly recognized, yet, their impact on SE is largely unknown. We undertook this study to determine the prevalence of inflammatory SE and assess related demographical features and outcome.

Methods: This was a retrospective analysis of a prospective registry of adult SE patients treated in our center, from 2008 to 2014, excluding post-anoxic causes. We classified SE episodes into three etiological categories: infectious (related to direct infection of the brain, such as viral, bacterial or parasitic meningo-encephalitis, acute abscess or empyema, prion disease), autoimmune (such as due to antibody-mediated autoimmune encephalitis, Rasmussen encephalitis, multiple sclerosis) and non-inflammatory SE. Demographical and clinical variables were analyzed regarding their relationship to etiologies and functional outcome.

Results: Among the 570 SE episodes, 33 (6%) were inflammatory (2.5% autoimmune; 3.3% infectious). Inflammatory SE episodes involved younger patients (mean, 53 versus 61 years, p=0.015) and were more often refractory to initial antiepileptic treatment (58% versus 38%, p=0.041), despite similar clinical outcome. There was no substantial difference between the two groups concerning gender, presence of seizures prior to the SE episode, seizure type, SE severity score (STESS), need of pharmacological coma-induction for treatment. Subgroup analysis showed that, as compared to autoimmune SE episodes, infectious SE involved older adults (mean, 60 versus 44 years, p=0.017) and was associated with higher morbidity (new handicap at discharge in 53% versus 21% of cases, p=0.043), without any difference in mortality.

Conclusions: Despite increasing awareness, inflammatory SE etiologies were relatively rare over the last years; occurrence in younger subjects and higher refractoriness to treatment did not have any impact on outcome. Autoimmune episodes also occurred in younger patients, but tended to have better outcomes in survivors than infectious SE.

P39

Super-refractory nonconvulsive status epilepticus secondary to fat emboli: a clinical, electrophysiological and neuropathological study

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Background: Fat embolism syndrome (FES) is a rare complication of long-bone fractures and joint reconstruction surgery. To the best of our knowledge, we describe the clinical electrophysiological, neuroimaging and neuropathological features of the first case of super-refractory nonconvulsive status epilepticus (sr-NCSE) secondary to fat emboli.

Methods: Clinical, continuous video-electroencephalograhy (v-EEG), neuroimaging and neuropathological data are described in detail.

Results: An 82-year-old woman was transferred to our intensive care unit because of sudden decrease of consciousness level, right hemiparesis and acute respiratory failure in the early postoperative of knee prosthesis surgery. Brain Computed Tomography (TC) including angio-CT and CT perfusion were normal. An urgent v-EEG showed continuous sharp-slow wave complexes at 2-2.5 Hz in keeping with the diagnosis of generalized NCSE. Epileptiform discharges ceased after the administration of 5 mg of intravenous diazepam, and background activity constituted by diffuse theta waves was observed. Treatment with levetiracetam (1000 mg/day) and sedation with propofol and midazolam was initiated. Moreover, continuous v-EEG monitoring was also started. Despite antiepileptic therapy, epileptiform activity recurred after the interruption of profound sedation, and valproate and lacosamide were added during the ensuing days. Magnetic Resonance Imaging (MRI) showed multifocal punctate areas of hyperintensity on the T2-weighted and FLAIR images in both the deep gray and subcortical white matter. NCSE remained without control for 2 weeks. Given the advanced age of the patient, the family refused further aggressive intervention. Finally, the patient died. The clinical autopsy revealed a pulmonary fat embolism associated with hemorrhagic infarction in the left lower lobe. Fatty lesions were also seen in the intestine and pancreas. Scattered microscopic cerebral infarcts associated with fat emboli in the capillaries were seen affecting both supra and infratentorial structures.

Conclusions: Fat emboli should be considered a potentially cause of sr-NCSE.

P40

HHV-6 encephalitis after allogeneic stem cell transplant: balancing therapy and toxicity

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Background: HHV-6 is a ubiquitous double-stranded beta-herpesvirus with A and B variants. HHV-6A is thought to be more virulent and neurotropic; exact transmission mode is unknown. HHV-6B causes exanthema subitum, and has been associated with febrile seizures and possibly later development of mesial temporal sclerosis due to latent reactivation. HHV-6B is associated with limbic encephalitis in immunocompromised patients, particularly those undergoing allogeneic hematopoietic stem cell or solid organ transplantation.

Case: A six-year-old boy with X-linked chronic granulomatous disease had allogeneic matched unrelated stem cell transplant from peripheral blood in 8/2012, and modified boost stem cell transplant in 4/2014 after graft failure. He developed status epilepticus with continuous bifrontal epileptiform discharges. He was treated with levetiracetam, midazolam, fosphenytoin, phenobarbital, and pentobarbital coma with burst suppression. MRI showed bilateral hippocampal diffusion restriction on DWI/ADC and bilateral hippocampal FLAIR increases. Lumbar puncture: WBC 9 (93% lymphs), RBC 1, gluc 56, prot 22. HHV-6 PCR positive: 94,300 copies/mL (HHV-6B). Serum HHV-6: 242,150 copies/mL (HHV-6B). He was started on foscarnet and ganciclovir with serological response. Repeat LP HHV-6B 1700. Weaned from pentobarbital slowly over 1.5 weeks, he developed cardiomyopathy (related possibly to phenobarbital), pulmonary failure (multifactorial pneumonia), renal failure (multifactorial, possibly related to foscarnet) requiring continuous veno-venous hemodialysis, and hepatic failure (veno-occlusive disease vs GVHD). Terminally, he developed intractable hypoxemia. Serum HHV-6B was < 250 copies / ml, and CSF 1700-5000 copies/ml, but autopsy showed > 3,000,000 viral copies/10^6 cells in hippocampus, and 383,673 in lung on digital droplet PCR, a sensitive HHV6 detection technique.

Conclusion: In this case, although clinical and electrographic seizures were controlled, virulent HHV-6B CNS and systemic infection persisted, despite low peripheral levels, that did not correlate with ongoing active CNS infection. Neither anti-seizure nor anti-viral therapy modified the course of the disease.

P41

Treatment non-adherence as a trigger of status epilepticus

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Background: Non-adherence to antiepileptic drug treatment is a major trigger of status epilepticus in patients with established epilepsy. We wished to assess the extent of this problem by means of therapeutic drug monitoring.

Methods: A total of 124 consecutive admissions for status epilepticus in patients with established epilepsy were studied. Non-adherence was defined as having a serum concentration/dose ratio at admission of <75 % of the patient's own control value.

Results: In 64 cases serum concentration/dose ratios at admission were available for comparison with trough control values. Treatment non-adherence was identified in altogether 24 (38%), 50 % in children, 32 % in patients 16 - 59 years and in 44 % above 60. Missed medication had been reported in only two of these patients. No significant associations with demographic factors or epilepsy and status epilepticus characteristics were found. No cases with confirmed non-adherence had a fatal outcome.

Conclusion: Antiepileptic drug non-adherence is a common cause of status epilepticus across all ages, but is not always identified as history-based information is often inaccurate. Prompt and reliable identification of non-adherence is imperative for correct management. Non-adherence should always be in focus when seizure aggravation occurs in patients with epilepsy. This is the first study to demonstrate the extent of non-adherence by therapeutic drug monitoring in status epilepticus.

P42

Recurrent non-convulsive status epilepticus in a patient with progressive left hemispheric leukoencephalopathy after a remote viral meningoencephalitis

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Nonconvulsive status epilepticus (NCSE), defined as changes in behavior and/or mental processes from baseline with continuous epileptiform discharges, remains a diagnostic and treatment challenge. Here we present a 68 year-old female who developed 3 episodes of NCSE 10 years after a viral meningoencephalitis and gradually progressed to left hemispheric leukoencephalopathy.

This patient had no major medical illness prior to her viral meningoencephalitis in 2001. She recovered completely from the infection and remained well until Nov 2010, when she became confused after a urinary tract infection. Cerebrospinal fluid (CSF) study and brain MRI were unremarkable. EEG showed diffuse slow waves when she was confused and showed focal sharp waves at F3C3 when she was clear 10 days after. The second episode was on Aug 2012, presented with fever, acute mental change up to 2 weeks, abnormal gazing and nystagmoid like movements, aphasia, right hemiparesis after several episodes of myoclonic jerks. Brain MRI revealed white matter changes and a small high signal intensity lesion at left frontal cortex in DWI. EEG showed continuous periodic lateralized epileptiform discharges at the left hemisphere. She responded well to levitiracetam and recovered completely to

her usual state within 2 months.The third episode was on Nov 2013, after a vaccination and urinary tract infection, presented with right hemiplegia, global aphasia, and persistent drowsiness. EEG showed left frontocentral epileptic discharge, MRI showed extensive left hemisphere leukoencephlopathy. CSF study and autoimmune profile including NMDA, AMPA 1, AMPA2, GABA, LGI1, CASPR2 were all negative. Corticosteroid and zonisamide were added with levitiracetam. She is still aphasic but could walk with some support 1 year later.
In this case, we hypothesize that immune mediated mechanisms, and perhaps genetic predisposition have something to do with epileptogenesis as well as NCSE, and these will be discussed.

P43

A super- refractory status epilepticus occurring during labor

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The super-refractory Status Epilepticus (SE) is defined as a state that continues or recurs for at least 24 hours despite the administration of general anesthetics. Diagnostic and therapeutic management requires a coordinated multidisciplinary approach in an intensive care environment. The exact prevalence is unknown, from numerous/various prospective studies it can be estimated that 22% of SE does not respond to first and second level treatment and 41% of these require the administration of anesthetics to medically induce coma.

Case description: A 22 year old woman at 41 weeks of a normal course pregnancy, with an apparently negative medical and pharmacological history, presented a first epileptic seizure immediately after the induction of non-pharmacological labor. The seizure was characterized by a scream followed by right side clonic seizures, the next generalization is not certain. A second seizure recurred upon waking from the anesthesia used for the cesarean section. An epilepticus status was suspected and the patient was admitted to the ICU, where she was initially treated with magnesium, general anesthetics (midazolam, propofol and thiopental) and then with anti-epileptic drugs (PHT, Lacosamide, PB, VPA, LVT). SE of the left focal, sometimes secondarily generalized, persisted for the 29 days of hospitalization, a video-EEG was recorded for most of that time. Three brain MRIs were performed that showed a large area of altered signal in the left temporal-parietal-occipital and thalamus lobes at outcome, minimum gliosis after about three months. The search for etiological causes was carried out following the most likely hypothesis: eclampsia, embolic stroke or cerebral venous thrombosis, CNS infection, and paraneoplastic autoimmune diseases. This last hypothesis seemed confirmed by clinical and EEG prompt response to the administration of high-dose IV methylprednisolone. The serum research for various autoantibodies was positive for Antibodies to Endothelial Cells. Currently the patient, in polytherapy with PB, LVT, VPA, presents brief critical episodes in falling asleep about every 20 days and a severe dystonia of the right hand that is activated with concentration. The EEG shows left hemispherical lens abnormalities.

Conclusions: The etiological diagnosis is critical for the therapeutic management of super-refractory SE. Autoimmune diseases may represent a possible diagnosis and should always be considered and monitored over time, even for their prognostic significance (possible paraneoplastic manifestation).

P44

Status Epilepticus Cases Arising in Connection to Non-Convulsive Cephalosporin

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Background: Cephalosporins are beta-lactam antibiotics which can cause neurotoxic side effects. It is argued that these drugs reduce the neuronal excitability threshold acting as GABA antagonist during the pathophysiological processes. Non-convulsive status epilepticus (NCSE), unlike the normal state is defined as higher cortical function changes lasting more than 30 minutes where tonic, clonic or tonic-clonic founding was not observed.

Methods: Five patients evaluated as NCSE whose kidney functions are impair and using cephalosporin.

Case-1: A 49-year-old male patient was monitored for the reason of the value rise in urea, creatinine. On the 3rd-day of the cefazolin antibiotic it was observed in the EEG that the patient who was disoriented and agitated was in the NCSE status. Benzodiazepines were administered and cefazolin therapy was discontinued. About a week later, remission in his neuropsychological examination was observed in the patient's clinical findings.

Case-2: A 37-year-old female patient have ankylosing spondylitis and chronic renal failure (CRF). The cefepime therapy the patient developed loss of orientation and somnolence. It was observed in NCSE. Benzodiazepines were administered and cefazolin therapy was discontinued. The patient recovered after the treatment.

Case-3: A 24-year-old female patient have lupus nephritis depending on CRF. On the 3rdday of the ceftriaxone treatment, she developed confusion. Status treatment protocol was applied. The patient recovered after the treatment.

Case-4: A 58-year-old female patient was monitored because of mesothelioma, diabetes mellitus, and CRF. Cefepime therapy was discontinued with the patient who was NCSE compatible. Status treatment protocol was applied. The patient recovered after the treatment.

Case-5: A 51-year-old male patient who had colon carcinoma, urea, and creatinine height developed high fever after the operation.Taking the patients wound infection into consideration ceftriaxone 2g/day was started. Status treatment protocol was applied.

Results and Conclusions: NCSE and seizures can be seen after treatment cefazolin, cefuroxime, ceftazidime and cefepime.The risk of neurotoxic side effects was increased in patients with low creatinine clearance. Therefore, NCSE diagnosis should be considered with patients who have chronic renal failure and take cephalosporin group of antibiotics when there is a change in awareness. EEG diagnosis must be necessarily made.

P45

Infraslow status epilepticus: A new form of subclinical status epilepticus

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Background: Analysis of infraslow EEG activity (ISA) has shown potential in the evaluation of patients with epilepsy and in differentiating between focal and generalized epilepsies. Infraslow EEG activity analysis may also provide insights into the pathophysiology of refractory clinincal and subclinical status epilepticus
The purpose of this report is to present a girl with Sturge-Weber Syndrome (SWS) who presented with a 96-hr refractory encephalopathy and non-ischemic hemiparesis who was identified to have infraslow status epilepticus (ISSE), which successfully resolved after Midazolam administration

Methods: The continuous EEG recording of a 5-yr-old girl with known Structura Epilepsy due to Sturge-Weber is presented. The patient presented to the ED with acute confusion, eye deviation and right hemiparesis similar to

two previous admissions. Despite lorazepam, fosphenytoin, phenobarbital and valproic loads the patient showed no improvement of the clinical condition after 96-hour. The continuous Video EEG monitoring (VEM) showed continuous severe diffuse asymmetric slowing but no apparent ictal activity on conventional EEG recording settings. As a brain CT, CTA, CTV and complete MRI including DWI obtained within 72-hr of presentation failed to demonstrate any ischemic changes, analysis of the EEG nfraslow (ISA) activity was undertaken using LFF 0.01 AND HFF of 0.1 Hz respectively.

Results: Continuous subclinical unilateral rhythmic ictal ISA was identified. This was only evident in the left hemisphere which correlated with the structural changes due to SWS. A trial of continuous 120- to 240 ug/kg/hr of IV midazolam resulted in immediate resolution of the contralateral hemiparesis and encephalopathy.

Conclusion: Continuous prolonged rhythmic ictal Infraslow activity (ISA) causes super-refractory subclinical focal status epilepticus. This has not previously reported, and propose this should be called infraslow status epilepticus (ISSE). ISA analysis should be performed in all patients with unexplained subclinical status epilepticus.

P46

Effect of antiepileptic drugs on clusters of treatment resistant absence seizures - a video EEG monitored response

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We report a case of a 45 year-old female with 38 years history of treatment resistant absence seizures. Attacks occurred up to 300 times a day significantly affecting daily activities and quality of life. Drug history: Na Valproate, Ethosuximide, Lamotrigine, Levetiracetam, Clonazepan and others. In 2001 a VNS was inserted, without treatment benefit. The patient (pt) at this time resorted to consulting the Internet and started dexamphetamine (DA) against medical advice.

To assess ictal frequency on DA and treatment response to new AEDs a 96h in-patient EEG video telemetry was arranged. During monitoring pt was aware of 15% of generalized 3 (range 2-4) Hz spike/polispike and wave discharges lasting up to 7 seconds. Day 1: on 15mg am and 10mg lunchtime DA 348 EEG and 69 pt events were recorded over 24h. Day 2: 10mg am DA EEG events reduced to 326, while pt events increased to 93 over 24h. Day 3: 10mg DA and 50 mg Lacosamide (LCS) am, followed by a 100 mg noon and 50mg pm LCS dose was associated with 374 EEG and 161 pt events over 24h. Day 4: 100mg am modafinil (Mod) reduced daytime EEG events to 4-9/hour and pt events to 35; evening 800mg Eslicarbazepine increased EEG events to 17-34/ hour and pt events to 100 in sleep. Day 5: 100mg am and noon Mod reproduced benefit of day 4, the addition of 500mg Ethosuximide 4pm led to 53 (0-10/h) EEG events between 4pm and 6am. Discharges were fewer and shorter, pt events however only reduced to 78 over 24h. Day 6: 2 mg Perampanel am was followed by 1-18 EEG events/h. Recording was terminated 10h after dose.

Our model objectively documented seizure frequency in an adult with absences. Data collected suggest best response to Modafinil and Ethosuximide. Case reports (D'Orsi et al. Seizure, 2014) document Lacosamide may be effective for absence status, we could not replicate this. Eslicarbazepine caused worsening seizure control and data on Perampanel were insufficient to draw a conclusion.

P47

Assessment of the timeliness of administration of second line antiepileptic drugs for status epilepticus after the implementation of a status epilepticus bundle order Set: a single institution experience

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Objective: To determine if there is improvement in the average time of administration of second line anti-epileptic drugs (AED) in status epilepticus (SE) following the implementation of a Status Bundle Order Set (SBOS).

Background: Status epilepticus (SE) is a neurological emergency associated with significant morbidity and mortality. First line of treatment includes benzodiazepines use. A prior study at the University of Kentucky found a delay greater than 1 hour in administration of the second line AED for SE. Strategies were proposed and the use of an order set was adopted.

Methods: This is a retrospective chart review of adult patients 18 years and older. Several months after the implementation of a SBOS, cases of SE were identified during the month of August 2014. Time to administer of second line AED was assessed from the time the AED order placement to the time the patient received the medication.

Results: Seven cases of SE were identified with an average AED administration time of 82 minutes (SD 32). STAT orders were completed before ROUTINE orders on average of 71 minutes vs 96 minutes respectively. Delays in AED administration were noted at several levels: at the physician level while placing the order, at the pharmacy level while admixing and delivering the AED, and at the nursing level while administering the AED.

Conclusions: Despite the creation of a SE bundle order set significant delays in second line AEDs continue to be identified. These delays in timeliness of AED administration lead to the development of an enterprise wide SE Alert Protocol which will include a bedside response team. The data following its implementation will be presented at the AAN meeting.

P48

Safety and pharmacokinetics of IV loading dose of Lacosamide in the ICU

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Rationale: Lacosamide (LCS) is a relatively new antiepileptic drug available for intravenous administration which has been reported last year to be a fast, effective and safe alternative in emergency situations. This warrants further investigation to better understand the safety and doses which can be used in this situation.

Methods: With IRB approval, patients were identified that received IV LCS in the ICU for acute treatment of seizures in the past 18 months. Selected were those who were give an initial infusion of 400 mg or more. Data collected were age, gender, weight, duration of infusion, change or termination of infusion for side effects (e.g. hypotension), initiation of pressor agents during or up to 2 hrs after infusion completed. On a subset of 41 patients, LCS level had been obtained about 10 minutes after completion of infusion.

Results: Ninety four patients were identified. Demographics were male/female 48/46, average weight 82.0 kg (range 43.7 - 182.3), and average age was 56.1 yrs (24 - 83). Doses given were 400 mg (24 pts), 500 (4 pts), 600 mg (31 pts) and 800 mg (4 pts). Weight base dosing ranged was 2.68 to 13.60 mg/kg (ave 6.9). No patient had a change in 1) BP resulting in reduction in or stopping the infusion or 2) starting pressors. LCS levels were obtained in 51 patients post infusion. LCS level correlated well with weight based dosing. Doses above 7 mg/kg produced le-

vels of 10 ug/ml. Average volume of distribution was 0.57 L/Kg.

Conclusions: Loading doses of IV LCS can be safely given up to 1100 mg and 13 mg/kg over 30 min. Vd found in ICU patients (0.58) is similar to reported value of 0.6 L/K in healthy volunteers. Weight based dosing should be used to achieve a target plasma level. Steady state LCS levels reported in clinical trials with 200, 400 and 600 mg per day are 4.99, 9.35 and 12.46 u/ml. To achieve high "therapeutic" level post IV load, doses of 8-10 mg/kg should be used which we found to be safe to use.

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Comparison of the effectiveness of four antiepileptic drugs in treatment of status epilepticus according to four different efficacy criteria

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Background: The preliminary data presented here shall give an impression on how different criteria for the identification of an antiepileptic drug (AED) with a possible or certain treatment effect can have an influence on the results of retrospective case series.

Methods: We present a data subset from a large retrospective study, which when completed will cover all treatment episodes of SE at the neurological department of the University of Rostock hospital from January 2010 to June 2013. We compare and contrast the results of four different efficacy criteria for the effectiveness of Phenytoin (PHT), Valproate (VPA), Levetiracetame (LEV) and Lacosamide (LCM). Criterium 1 = the last AED administered before SE termination. Criterium 2 = the last drug introduced into the antiepileptic therapy within 72 hours before the cease of the SE and without changes in the co-medication. Criterium 3 = the last drug introduced into the antiepileptic therapy or increased in dose within 24 hours before termination of the SE without changes in the co-medication. Criterium 4 = the last drug introduced into the antiepileptic therapy within 72 hours before the cease of the SE even allowing changes in the co-medication.

Results: 28 treatment episodes in 24 patients (9 male, 14 female, mean age at first episode 69 years SD 16) could be analysed. In 24 episodes at least one AED was given intravenously (i.e. PHT n = 10, VPA n = 17, LEV n = 19, LCM n = 6). Efficacy rates according to all four criteria were not significantly different between the four AEDs, but the efficacy rates of each AED differed considerably when using different efficacy criteria (e.g. LEV criterium 1 efficacy rate 47.4%, criterium 2 efficacy rate 15.8%).

Conclusion: Efficacy criteria for the effectiveness of AEDs in the treatment of SE should be standardized.

P50

Treatment with perampanel in patients with refractory status epilepticus on a neurological intensive care unit

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Objective: In refractory status epilepticus (SE), due to subcellular maladaptive changes, GABAergic drugs are no longer effective and the excitatory neurotransmitter glutamate (Glu) plays a major role in seizure perpetuation. Perampanel (PER, licensed since 09/2012) is the first orally active non-competitive AMPA receptor antagonist for adjunctive treatment of refractory focal epilepsy.

Methods: We analysed treatment response, seizure outcome, and adverse effects of add-on treatment with perampanel in patients with refractory status epilepticus on the Neurological Intensive Care Unit (NICU), Salzburg, Austria between 09/2012 and 11/2014 by retrospective chart review.

Results: Twelve patients (75% women) with refractory status epilepticus were treated with PER administered per nasogastral tube on the NICU between 09/2012 and 11/2014. Median age was 74.6yrs [range 59.7-90.5; SD 10.8]. The most frequent SE type was non-convulsive SE (NCSE) with (6/12, 50%) and without coma (4/12, 33%). In the majority of pts. (8/12, 67%) SE arose de novo, with an acute symptomatic cause in five pts (42%). Cerebrovascular diseases (4/12; 33%) and cerebral tumors (4/12; 33%) were the most common etiologies. SE lasted less than 24 hours in 7 pts (58%), one to seven days in three pts. (25%) and more than 7 days in two pts. (17%). PER was given after a median number of four antiepileptic drugs [range 2-7] and a median time of 1.5 days [range 0.8-18.3]. In two pts. (17%) clinical improvement could be observed after administration of PER without correlating EEG changes. Median initial dose was 4 mg [range 2-12; SD 4.11], titrated up to median 12 mg [range 4-12] in steps of 2 to 4 mg per day. No adverse effects were reported regarding cardio-respiratory changes or laboratory parameters. Outcome after SE was moderate disability in 5 pts. (42%), two pts. died (17%), two pts.(17%) remained in a persistent vegetative state.

Conclusion: Though glutamate plays a major role in seizure perpetuation, the non-competitive AMPA receptor antagonist PER was well tolerated, but could only ameliorate seizure activity in few patients with refractory SE. The long duration of SE before PER might have been responsible for the modest result.

P51

Water-soluble benzodiazepine prodrug/enzyme combinations for intranasal rescue therapies

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Background: Benzodiazepines (BDs) are the drugs of choice for rescue therapy. However, their poor water solubility has necessitated use of organic solvents in nasal formulations currently under development. These solvents cause irritation resulting in discomfort and, potentially, tissue injury. We propose the use of water-soluble BD prodrugs and corresponding converting enzymes, which when combined at the time of nasal administration produce rapidly absorbed super-saturated concentrations of the active medication.

Methods: Avizafone (AVF) is a water-soluble lysine prodrug that, when injected, is hydrolytically converted to diazepam (DZP). We screened a panel of enzymes to identify one or more that quickly convert AVF to DZP. A.O. protease from Aspergillus Orizae, having the optimal activity, was used to characterize the conversion kinetics of AVF. Next, we determined the DZP saturation concentration, which was used to calculate the ratio of AVF concentration relative to the DZP saturation concentration i.e. the supersaturation potential (S). Freshly mixed AVF/enzyme solutions of varying concentrations were then applied to the apical side of MDCKII-wt cell monolayers (an accepted nasal mucosa model) in a six well transport system.
Aliquots were collected at various times from both the apical and basal sides and assayed for AVF and DZP using HPLC.

Results: DZP solubility was 130±11 μM at pH 7.4 and 32°C. DZP conversion on the apical side occurred within a few minutes resulting in tenfold higher (supersaturated) concentrations than the saturation level. DZP flux across the MDCKII-wt membrane was proportional to S, for values up to 10 S, which was a tenfold improvement in absorption rate over saturated DZP. Negligible amounts of AVF crossed the membrane. No precipitates were observed and the cells remained viable.

Conclusions: DZP prodrug/enzyme combinations result in rapid DZP formation and absorption without use of organic solvents. This concept is applicable to other BD/enzyme combinations.

P52

Midazolam is effective in managing seizures during status epilepticus

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Status epilepticus is defined as a continuous convulsion lasting longer than 20 - 30 min or the occurrence of serial seizures between which there is no return of consciousness.
The incidence rate of status epilepticus is 15/100.000 habitants.
Aim of our study was to compare the efficacy of intravenous administration of Diazepam and Midazolam.

Result: During 2014 year we have treated 25 children with status epilepticus. 68% patients had acute infection or complication of febrile seizures, 25% had low anticonvulsant drug concentration and 7% had metabolic seizures. The mean age of patients was 3.7 years (range 6 month to 13 years). The type of seizure was generalized tonic – clonic at 19 patients, 3 partial, and 3 were complex partial seizures. Our institute for treatment of status epilepticus recommends the first line agent Diazepam, because it is fast acting and effective for all seizures types. We administrated intravenous Diazepam 0.2 – 0.3 mg/kg. When we didn't have control of seizures we repeated three times in five minutes intervals. Diazepam was effective at 17 patients. In other 8 patients we have continued with second line treatment drugs, infusion of Midazolam 50-300 μg/kg/h. The mean infusion duration of Midazolam was 10.5 hours (range 8 – 24 hours). In two patient seizures did not stop after 24 hours, the patients needed mechanical ventilation, Thiopental infusion and support for hypotension.

Conclusion: Our results indicate that Midazolam is highly effective for the management of status epilepticus

P53

Pharmacologic treatment of neonatal seizure in Chungbuk, Korea

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Neonatal seizures are the most important indicator of neurologic dysfunction in the neonatal period. A mainstay in the therapy of neonatal seizures is the diagnosis and treatment of underlying etiology. So we studied treatment of neonatal seizure in Chungbuk Korea.
We retrospectively studied the type of epilepsy, etiology, EEG, brain sono, antiepileptic drug, doses of drug. We studied 10 neonate treated neonatal seizure who visited our hospital since January 2011 to December 2013.

The mean age to admit initially is 8±9 days(from 1 days to 21 days). The male is 5 and female is 5. The myoclonic seizures is 5, tonic seizure is 3, apnea is 1 and subtle seizure is 1. The etiology of neonatal seizure is that hypocalcemia is 5, intracranial hemorrage is 1 and hypoxic ischemic encephalopathy is 1. The Brain sono is that germinal matrix hemorrhage with IVH is 1 and diffuse echogenecity periventricular white matter of lateral ventricle is 1. Abnormal EEG is 70%. The treatment is that phenobarbital is 7. The mean maintenance dose is 5±4 mg/kg/day The mean duration of therapy is 1±2 months, and the duration of therapy ranged from 1 to 3 months. 90.0% of patients became seizure free.
We studied treatment of neonatal seizure: A systemic review. Phenobarbital is effective and tolerable in neonatal seizure in Korea. The further study is necessary about other antiepileptic drug.

P54

The established status epilepticus treatment trial (ESETT): design and status

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Background: Fosphenytoin (FOS), valproic acid (VPA), and levetiracetam (LEV) are all commonly used to treat adult and pediatric patients with generalized convulsive status epilepticus that remains refractory to benzodiazepines. However, the efficacy and safety of these drugs, both absolute and relative, in this population remain untested in adequate and well-controlled randomized trials.

Methods: ESETT is an ongoing multicenter, randomized, blinded comparative effectiveness study of fosphenytoin, valproic acid, or levetiracetam in the emergency department treatment of patients with benzodiazepine-refractory status epilepticus. It is funded by the U.S. National Institutes of Health. Eligible patients will be enrolled with exception to informed consent (EFIC) and randomly assigned to FOS 20 mgPE/kg, LEV 60 mg/kg or VPA 40 mg/kg, which will be administered over 10 minutes. The primary outcome is clinical cessation of status epilepticus, determined by the absence of clinically apparent seizures and improving responsiveness, at 60 minutes after the start of study drug infusion, without the use of additional anti-seizure medication. After 300 enrollments, response adaptive randomization will be used with the goal of maximizing the likelihood of identifying the most effective treatment

arm, up to a maximum of 795 enrollments over 4 years. The trial operating characteristics for this adaptive design were optimized to identify a 15% minimally clinically important difference via an extensive simulation study, which ensures the type I error probability is less than 0.05 under a variety of scenarios.

Status: Following scientific peer review and regulatory review, the study was funded in the fourth quarter of 2014. Study drug manufacturing and testing is underway. Clinical sites are engaged in the community consultation and public disclosure required for EFIC in the US, and are preparing to begin enrollment in the third quarter of 2015.

Conclusions: ESETT will determine the probability of each agent being the most or least effective. It will be a success if either is greater than 0.975 for any treatment. At the conclusion of the trial, we will report the response rates for each treatment group with 95% credible intervals and the pairwise differences in responses rates and corresponding 95% intervals of those differences.

P55

Factors associated with poor discharge status in patients with status epilepticus at Khon Kaen Hospital

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Background: Status epilepticus (SE) is a serious neurological condition and has high a mortality rate. Factors associated with poor outcomes in Asian or Thai populations are limited.

Methods: Adult patients diagnosed as SE at Khon Kaen hospital, Thailand from October 1st, 2010 to September 30th, 2012 were enrolled. Patients were categorized as good or poor outcomes at discharge. Poor outcome was defined as not improved/discharged against advice death or presence of a neurological deficit. Clinical factors were compared between both groups.

Results: During the study period, there were 211 patients diagnosed as SE. Of those, 130 patients were male (61.61%). The mean age of all patients was 53.28 years. Acute stroke was the most common cause of SE in 33 patients (15.64%). At discharge, there were 91 patients (43.13%) who had poor outcomes. Only plasma glucose was significantly associated with poor outcomes with an adjusted OR of 1.012 (95% CI of 1.003 and 1.021).

Conclusions: Plasma glucose is associated with poor discharge status in patients with SE. Glucose control during SE may be beneficial.

P56

Factors related to delays in pre-hospital management of status epilepticus

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Background: Status epilepticus (SE) is a life-threatening emergency situation requiring immediate action. A recent study shows unacceptably long treatment and diagnostic delays in the management of SE. This study was designed to identify factors related to delays in pre-hospital management of SE, in order to detect the means to reduce delays in pre-hospital, diagnostic and third-stage treatment procedures.

Methods: This retrospective study includes all adult (>16 years) patients (N=82) diagnosed with SE in Helsinki University Central Hospital emergency department over 2 years. We collected 15 SE type-, patient- and SE episode-related variables from the medical records and counted six delays in pre-hospital setting and analyzed their relations with univariate analysis and multivariate linear regression models.

Results: In the multivariate regression analysis focal SE was significantly associated with long onset-to-initial-treatment ($p<0.05$), onset-to-diagnosis ($0<0.002$) and onset-to-anesthesia ($p<0.002$) delays. Administration of the initial treatment before EMS arrived was significantly associated with long onset-to-alarm ($p<0.02$) and onset-to-first-ED ($p<0.04$) delays. Primary admission to a healthcare unit other than tertiary hospital caused a significant delay in diagnosis ($p<0.008$) and anesthesia ($p<0.02$). Surprisingly, univariate analysis revealed that if SE onset occurred in a healthcare unit, the onset-to-alarm ($p<0.001$), onset-to-first-ED ($p<0.001$), onset-to-tertiary-hospital ($p<0.001$), onset-to-diagnosis ($p<0.02$) and onset-to-anesthesia ($p<0.01$) delays were significantly longer, as compared to SE onset at a public place.

Conclusion: We found remarkable inadequacy in recognition of SE both among laity and medical professionals. There is an obvious need for increasing awareness of imminent SE and optimizing the pre-hospital management of established SE with streamlined standard management protocol. To ensure rapid diagnosis of SE, we recommend more frequent response with physician-based EMS upon alarms indicating prolonged seizure, investigation of the possibilities of eEEG recording on emergency site, and triaging SE patients exclusively to hospitals with competence for neurological intensive care.

P57

Predictors of status epilepticus duration and short-term outcome in Bulgarian patients treated in a neuro-intensive care unit

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Background: Status epilepticus (SE) is a life-threatening condition of ongoing or repetitive seizures which carries high mortality and severe disability. Our purpose was to identify predictors of SE duration and short-term outcome.

Methods: We performed a prospective study of 95 consecutive patients diagnosed with SE and treated in a neuro-intensive care unit over a period of 3 years. Demographics and clinical data concerning established epilepsy and SE were collected and their relationship to SE duration and short-term outcome was analyzed. SE short-term outcome assessment was based on the rate of recurrent seizures during hospitalization and functional recovery according to the Glasgow Outcome Scale results.

Results: The longer SE duration was more frequent in cases with non-convulsive SE, SE polytherapy, abnormal EEG findings after SE management, prior partial epilepsy with polymorphic seizures. The predictive role of SE type, SE treatment, and prior epilepsy seizure type for SE duration was confirmed on multivariate analysis $P < 0.001$ ($F = 10.89$). The rate of seizure recurrence was significantly higher in participants with longer duration of prior epilepsy and SE, SE polytherapy, previous SE episodes, established epilepsy with polymorphic seizures, poor compliance and inadequate antiepileptic treatment. On multivariate regression analysis the predictive role of prior epilepsy duration and SE duration for seizure recurrence was confirmed $P < 0.001$ ($F = 14.52$). The unfavorable functional outcome correlated with older age, existing neurological abnormalities, mental retardation, prior symptomatic epilepsy, remote symptomatic etiology of SE, non-convulsive SE, and longer duration of SE. Existing neurological abnormalities, mental retardation, SE etiology and duration were confirmed as functional recovery predictors on multivariate ana-

lysis P < 0.001 (F = 16.70).

Conclusion: The study confirms the predictive value of some clinical factors for SE duration and short-term outcome. Our results are useful for finding more successful strategies in SE management.

P58

Prognosis of status epilepticus (SE): relationship between SE duration and subsequent development of epilepsy

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In animal models SE duration is related to epileptogenesis. Data in humans are scarce, mainly in NCSE, therefore we aimed to study the prognosis of SE de novo and which factors may influence subsequent development of epilepsy.

Methods: We evaluated SE patients without previous epilepsy at our hospital (February 2011-February 2014), including demographics, etiology, number of AEDs, duration of SE, mortality and occurrence of seizures during follow-up.

Results: 89 patients were evaluated. Median age was 69(19-95). 70.8% were convulsive. Regarding etiology, 59 were considered acute symptomatic (41 lesions, 18 toxic-metabolic), 17 remote or progressive symptomatic and 13 cryptogenic. The median recovery time was 24 hours (30 min-360 hours). In-hospital mortality was 29% (n=26). After a median follow-up of 10 months, 58.7% of survivors (n=37) showed seizures. Subsequently, we analyzed which factors might be related to the development of epilepsy, and we found that it was more frequent in longer SE (37 vs. 23 hours, p=0.004); furthermore, patients with a toxic-metabolic etiology developed less frequently epilepsy (33% vs. 67%; p=0.022). Epilepsy was also correlated (tendency) with focal SE (p=0.073), a lesion in neuroimaging (p=0.091) and the use of 2 or more AEDs (p=0.098). Regarding SE duration, a cutoff above 24 hours was clearly related to chronic seizures (p=0.014); however, combining etiology and duration, the association of longer SE and epilepsy was significant in acute lesional SE (p=0.034), but not in patients with cryptogenic or remote/progressive etiology. After a logistic regression, only a duration longer than 24 hours (OR 3.800 (1.277-11.312), p=0.016) was found to be independent predictor of development of epilepsy.

Conclusion: In SE patients, the longer duration is associated with an increased risk of subsequent epilepsy at follow-up, mainly in symptomatic SE due to an acute lesion. A more aggressive treatment might arise in this group to avoid this possibility. Most of the patients with cryptogenic or remote/progressive SE developed epilepsy independently of duration.

P59

A new clinical score for prognosis of status epilepticus

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Purpose: Status epilepticus(SE) has an important clinical impact, with a short-term mortality.
The Status Epilepticus Severity Score(STESS) is the only available scoring system to predict mortality in SE, using four variables available at presentation: history of seizures, age, seizure type, and consciousness impairment.
The baseline modifed Rankin Scale (mRS) might be a pronostic factor for short-tem outcome of SE, therefore our aim was to evaluate this association and to asses if the addition of this item to STESS, improves the prediction of mortality.

Methods: We collected consecutive patients with SE> 16 years old at our center between March 2011 and March 2014. Patients with post-anoxic SE were not included.
We performed ROC curves and a logistic regression model to estimate the scores of the new scale (modified STESS) and the comparison with the classic STESS

Results: We included 136 patients. Mean age: 62.01 ± 17.62[19-95]. 54.4% male.
The capability of STESS to predict mortality was 74,3%(IC: 63,8-81,8 %) and for the mRS was 65,2%(IC: 54,2-76,2%); both variables were independent predictors of mortality.
The coefficients of the logistic regression model and results of ROC curves allowed us to classify mRS as follows: 0 (mRS=0); 1 (mRS=1 to 3) and 2 (mRS>3); these values combined with the other items of classic STESS results in a new scale with scores between 0 to 8 points (mSTESS).
The predictive capability of the new scale to predict mortality was 77.5%
mSTESS >4 established an overall accuracy of 81,1% to predict mortality, much higher than the overall accuracy of STESS ≥3 (59,6%)

Conclusion: The previous mRS was associated with the mortality risk. We propose a modification of STESS to include mRS to improve the prediction of mortality risk.

P60

Outcome following postanoxic status epilepticus in patients receiving controlled temperature after cardiac arrest

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Background: Postanoxic status epileticus has been considered as a strong predictor of poor outcome in comatose survivors of cardiac arrest (CA) receiving therapeutic hypothermia. However, recent data suggest that a subgroup of patients may recover. This study aims to evaluate relevant clinical and electrographic prognosis markers of a possible favorable outcome.

Methods: Retrospective study at a Swedish University hospital analysing all CA-patients receiving targeted temperature management at 33°C or 36 °C and simplified continuous EEG monitoring (cEEG) between January 2008 and Mars 2013. In patients who developed electrographic status epilepticus (ESE) the cEEG was reviewed retrospectively by a neurophysiologist blinded to the patient outcome. The EEG pattern prior to onset of ESE, duration of ESE, and, if tested, background reactivity to sound and pain stimuli was described systematically. Clinical findings, including clinical seizures, antiepileptic drugs, results from somatosensory evoked potentials (SSEP) and the value of neurone-specific enolase at 48 hours after CA were described in detail in the survivors of postanoxic status epilepticus. The antiepileptic treatment was not protocolized. To evaluate outcome the Cerebral Performance Category scale (CPC) was used at 6 months follow-up. Good outcome was defined as good cerebral performance (CPC 1) or moderate cerebral disability (CPC 2).

Results: Of the 148 patients, 40 (27%) patients developed electrographic status epilepticus. Twenty-five patients had discontinuous background prior to ESE. All of them died. Fifteen patients had continuous background prior to ESE. Four of them survived, three with CPC 1-2 and one with CPC 3 at 6 months. These patients developed ESE at a median of 46 hours after CA and three of them had a reactive EEG after normothermia. All of them had preserved N20 peaks on SSEP.

Conclusion: We conclude that a continuous EEG background before the onset of ESE and presence of EEG reactivity may be favorable factors for a good prognosis.

P61

Prognosis of GPEDs on first EEG in patients with hypoxic encephalopathy post cardiac arrest

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Background: The EEG, alongside clinical examination, imaging studies and SSEPs, is used to determine prognosis following hypoxic encephalopathy. Generalised periodic epileptiform discharges (GPEDs) are recognised to be a 'malignant' EEG pattern associated with very poor outcome with previous studies reporting no or few survivors. We looked at our database of cardiac arrest patients who subsequently developed GPEDs to determine clinical outcome and profile any survivors.

Methods: We identified all cardiac arrest patients treated at King's College Hospital between 2011-2014 who developed hypoxic encephalopathy associated with GPEDs, BiPLEDs (bilateral periodic epileptiform discharges) and periodic discharges on first EEG. We collected clinical data including age, gender, downtime, EEG reactivity, presence of seizures or myoclonus and outcome. Survivors were defined as patients who were discharged from hospital to home or neurorehabilitation unit.

Results: 36 post cardiac arrest patients with hypoxic encephalopathy were identified; 21/36 with GPEDs, 10/36 with BiPLEDs and 5/36 with periodic discharges on first EEG. The mean age of patients was 62.8± 14.5 years old, with 27 male (75%) and 9 female (25%). 10/36 patients survived, which is slightly higher than previously reported. Statistical tests to compare clinical characteristics between survivors and non-survivors demonstrated no significant difference except for presence of reactivity on first EEG (p=0.02). On discharge one survivor had good functional outcome (and subsequently became independent), but all others were dependent for all ADLs.

Conclusion: GPEDs carry a grave clinical prognosis following cardiac arrest. This study did identify a higher number of survivors compared to previous studies, but most were severely disabled at hospital discharge. Reactivity of the first EEG might predict better prognosis. We will try to follow up neurorehabilitation outcomes of survivors.

P62

Electrographic status epilepticus and neurobehavioral outcomes in critically ill children

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Background: Electrographic seizures (ES) and electrographic status epilepticus (ESE) are common in children in the pediatric intensive care unit (PICU) with acute neurologic conditions, and ESE is associated with worse functional and quality of life outcomes. As an exploratory study, we aimed to determine ESE was associated with worse outcomes using more detailed neurobehavioral measures.

Methods: 300 children with an acute encephalopathy underwent clinically indicated EEG monitoring and were enrolled in a prospective observational study. We obtained follow-up data from subjects who were neurodevelopmentally normal prior PICU admission. As an exploratory analysis, we evaluated for associations between seizure category and adaptive behavior (Adaptive Behavior Assessment System), behavioral and emotional problems (Child Behavior Checklist), and executive function (Behavior Rating Inventory of Executive Function) using linear regression analyses. A p-value of <0.05 was considered significant.

Results: We obtained full follow-up data for 32 of 137 (23%) subjects who were neurodevelopmentally normal prior to PICU admission and not known to be deceased prior to the follow-up study. The median duration to follow-up was 2.6 years (IQR 1.2-3.8). There were no differences in the acute care variables between subjects with and without follow-up data. Compared to patients without any seizures, ESE (coefficient -29.7, p=0.013) but not ES (coefficient -21.5, p=0.051) were associated with worse adaptive behavioral global composite scores. On multivariate analysis, when compared to subjects with no seizures, both ES (coefficient -28, p=0.014) and ESE (coefficient -36, p=0.003) were associated with worse adaptive behavioral global composite scores. Significant differences were not identified for total problem scores (ES coefficient -4.1, p=0.48; ESE coefficient 8.9, p=0.13) or global executive function scores (ES coefficient 2.1, p=0.78; ESE coefficient 14.1, p=0.06), although there were trends towards worse scores in subjects with ESE.

Conclusions: ES and ESE were associated worse adaptive behavior, and trends toward worse behavioral-emotional and executive problems. This was a small exploratory study, and the impact of ES and ESE on these neurobehavioral measures may be clarified by subsequent larger studies. However, these data suggest these neurobehavioral measures may be sensitive to outcome differences in future studies comparing various ESE identification and management strategies.

P63

Cerebrospinal fluid total tau protein as a biomarker in status epilepticus: a retrospective study

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Background: predicting status epilepticus (SE) outcomes is difficult, and primarily based on clinical and EEG parameters. To date, no reliable biomarkers exist to predict SE outcome. Tau protein is a phosphorilated microtubule-associated protein, principally localized at neuronal and axonal level in central nervous system (CNS). High total tau (t-tau) levels in CSF are related to neuronal and axonal damage. No study has specifically evaluated the prognostic value of CSF t-tau level in SE.

Methods: we retrospectively identified 24 patients with SE in an 8-years-long period. Exclusion criteria were acute structural brain damage as causative event of SE (acute symptomatic SE cases). All patients underwent lumbar puncture at SE onset or shortly after onset to exclude CNS infection. CSF t-tau level was measured in each patient and correlations with SE electro-clinical variables, response to treatment, neurological and epilepsy outcomes were analyzed. ELISA testing (Innotest hTau by Innogenetics, Gent, Belgium) was performed to quantify the concentration of the CSF biomarker.

Results: t-tau level was extremely high (>50000 pg/mL) in 6 patients, moderately high (between normal values and 50000 pg/mL) in 7 patients and normal in 11 patients. None of the patients presented CNS infection. A positive correlation between SE duration and t-tau was present. Out of 15 cases that resolved with anti-epileptic drugs (AED) treatment, 6 had moderately high t-tau levels, none had extremely high t-tau levels. Out of 9 cases that presented a refractory or super-refractory SE, 7 had pathological t-tau levels (extremely high in 6 patients). 30-day mortality was 2 in 11 cases with normal t-tau level and 3 in 13 cases with elevated t-tau levels. Surviving patients with pathological CSF t-tau had 50% chance of developing epilepsy at 6 months follow-up.

Conclusions: CSF t-tau seems to be a good candidate biomarker for SE severity. Moreover, the high probability to develop epilepsy in patients with higher t-tau suggests that it could be a reliable biomarker to predict chronic epilepsy after SE.

P64

A systematic review on the prognosis of convulsive status epilepticus

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Background: Convulsive Status Epilepticus is associated with significant morbidity and mortality. The duration at which a prolonged seizure is considered status epilepticus is somewhat arbitrary but a duration of 30 minutes is generally accepted. In the late 1990s an operational definition of status epilepticus was proposed whereby seizures persisting greater than 5-10 minutes were considered and treated as status epilepticus, potentially leading to more aggressive early treatment. The purpose of this study was to determine whether this had an impact on the prognosis of convulsive status epilepticus.

Methods: We carried out a systematic review from the 01/01/1990 up until 31/12/2014 to identify all cohort studies of patients presenting with status epilepticus published in English and French using Pubmed and Medline. Studies were subdivided into two subcategories (pre 01/01/2000 and post 01/01/2000 when the operational definition was adopted). Studies were similarly subdivided into paediatric and adult subcategories when appropriate. Only cohorts with greater than thirty patients with clear mortality/morbidity figures (30 day case fatality) were included. Case series of patients with status epilepticus secondary to a single aetiology were excluded.

Results: The results of the systematic review will be presented at the meeting.

Conclusion: If the results support our hypothesis that the associated mortality and morbidity has indeed decreased then it will further justify early aggressive treatment of prolonged seizures.

P65

Super refractory post-hypoxic myoclonic status epilepticus successfully treated with corticosteroids and Zonisamide. Case report

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Background: The acute post-hypoxic myoclonic status epilepticus (PMSE) is characterized by generalized myoclonic jerks in deeply comatose patients. PMSE predicts death or vegetative state in more than 90% of survivors.

Results: We present a case of an 18 year old women successfully treated for PMSE with add-on methylprednisolone sodium succinate (MP) and zonisamide (ZNS). The patient was admitted to the emergency unit after a near drowning accident and being approximately 15 minutes under water. The return of spontaneous circulation was achieved within 9 minutes followed by 24 hours hypothermia and sedation while continuous myoclonic jerks were observed. EEG showed myoclonic status epilepticus. She was treated with phenytoin, levetiracetam, lacosamide, clonazepam and phenobarbital, sedation with propofol and thiopental without any effect. Sensory evoked potentials were normal. MRI showed ischemic changes in the basal ganglia. The patient's clinical status fluctuated within short periods of time. Additionally gabapentin, baclofen, valproic acid were initiated without any effect. On the day 65, MP bolus of 1000 mg was administered for 3 days followed by gradual down titration. Furthermore, the patient was loaded with 200 mg ZNS and continued with 400 mg daily doses. Subsequent EEGs demonstrated pronounced background activity, with slowly diminishing spike activity. The patient has recovered after a long lasting rehabilitation with moderate neurological impairment.

Conclusions: Our case supports that methylprednisolone and zonisamide should also be considered in the treatment of refractory PMSE.

P66

Management of SRSE with Ketamine and/or Propofol

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Rationale: In addition to benzodiazepines, barbiturates and propofol: ketamine infusion is increasingly being used for management of Super Refractory Status Epilepticus (SRSE). Its unique mechanism of action (an NMDA antagonist) and a favorable hemodynamic profile of (increase in cardiac output, blood pressure) makes it a suitable agent for management of patients with hemodynamic instability. Our objectives were to study the resolution rates mortality rate of SRSE with ketamine infusion as adjunct to other AED's.

Methods: After IRB approval we reviewed the charts of 41 patients admitted to the Neurological ICU for management of SRSE between years 2010 and 2014 at Ochsner MC. Analysis included patients demographics, mortality rate, resolution of RSE, as and the dose range and duration of both ketamine and/or propofol infusions in combination or ketamine alone.

Results: Demographics - ages range was 25-89 years with 26 females and 15 males. NCSE was managed with a combination of propofol and ketamine (39) or ketamine alone (2). Ketamine infusion range from 25-175 mcg/kg/min (mKm) with a duration of 2 - 28 days. Propofol infusion range was 10 - 180 mKm with a duration of 0-41 days (duration of dual therapy varied from 0-26 days). We were able to achieve adequate control of SRSE in 40/36: resolution rate of 95%. The combination infusions, even for prolonged periods, did lead to some hemodynamic changes that were easily managed with aggressive fluid resuscitation and in some cases with vasoactive agents. The mortality rate was 15/41 (36%). Mortality resulted from with draw of care due to: a) severe initial neurological insult and poor prognosis and b) multi-system organ failure resulting from complications from anesthetics, or infections or underlying medical conditions.

Conclusions: Ketamine, with or without propofol, is effective in controlling SRSE. The hemodynamic profile of ketamine along with aggressive fluid resuscitation makes it a favorable agent for use in patients with RSE. In all but one, RSE was controlled with the combination of propofol and ketamine with rates ranged of 10-180 mKm and 25-175 mKm respectively without any treatment limiting side effects. This regimen can be an effective in the treatment of SRSE.

P67

Convulsive super refractory status epilepticus successfully treated with lacosamide. Case report

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Background: Super-refractory status epilepticus (SRSE) is defined as status epilepticus that continues 24 h or more after the onset of anaesthesia, including those cases in which the status epilepticus recurs on the reduction or withdrawal of anaesthesia'(Shorvon et al, 2012). SRSE is a severe condition, its no good prognosys consents the use of drugs with limited experience of efficacy as lacosamide.

Method and results: a 34 years old female, affected from pharmacoresistant focal epilepsy (daily seizures), mental retardation, psychiatric disorders and anorexia, was admitted (september 26, 2014) cause of continous versive seizures. Status was initially interrupted with 2000 mg of levetiracetam i.v. (she assumed VPA and PHT, the last used to stop a recent convulsive status epilepticus). The day after she had new seizures: transferred in ICU, was threated with continuous midazolam infusion for 24 h; transferred in our department, after 36 h showed new seizures. We transfered her again in ICU were was threated with midazolam and propofol without benefit, that induced to use TPS for 24 h with disappearance of seizures; during the gradual stopping of TPS was introduced 200 mg bid of iv lacosamide: EEG showed the resolution of electric epileptiform activity. Pt was delivered after 6 days, cause she was

seizure free, with 1000 mg of valproate and 400 mg of lacosamide. During last 3 months she had only 4 seizure.

Conclusion: the experience of lacosamide use in status epilepticus is until now limited, but our case represents a significant success not only for the contribution to stop status epilepticus. We signal this case for the role of LCS to stop a super refractory status epilepticus but also for the significative reduction of seizure frequence and disappearance of psychiatric disorders, included insomnia and anorexia.

P68

Stiripentol for the treatment of super-refractory status epilepticus

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Background: Stiripentol (STP) is likely to be effective in status epilepticus (SE) due to enhancement of inhibitory GABAergic neurotransmission. The objective of this study was to determine whether STP might be a treatment option in super-refractory status epilepticus (SRSE).

Methods: Medical records of patients treated due to a SE in Marburg between January 2013 and June 2014 were reviewed for administration of STP. Data collected included demographics, clinical diagnosis, etiology, semiology, previous seizures, length of stay, ventilation time, modified Rankin scale (mRS) and Status Epilepticus Severity Score. Primary outcome measures were EEG resolution of SE after initiation of STP.

Results: Five adult patients were started with STP due to SRSE. The median age was 78 years (interquartile range [IQR] 11 years), and four patients were female. The median duration of SRSE before initiation of STP was 39 days (IQR 16 days), and the median number of anticonvulsants used before was 6 (IQR 1). The patients were directly started on STP 2000 to 5000 mg/day, and titrated up to a maximal daily dose between 4000 and 6000 mg within 2–3 days. Lorazepam was administered at the same time at a median dose of 3 mg (range 1.5–6 mg). SRSE ceased in three patients within 2 to 4 days after the start of STP. Follow-up of 2 to 11 months showed that these three patients were able to return to a mRS of 1–3 and were tapered off to three AEDs only. In two patients, SRSE continued after administration of STP and further escalation of anticonvulsant regimen. Both were switched eventually to supportive care only. None serious side effects were observed while on STP.

Conclusions: Based on our presented cases and previous experimental animal data STP may prove useful in treating super-refractory SE (Class IV evidence). Prospective trials are warranted to examine the efficacy of the STP in adults with refractory SE and to examine if earlier treatment leads to better control of SE.

P69

Ketamine in refractory convulsive status epilepticus avoids endotracheal intubation

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Purpose: Conventional anaesthetics for treating refractory convulsive status epilepticus (RCSE) require endotracheal intubation, which increases the risk of morbidity and mortality. Ketamine is a non-conventional anaesthetic with increasing evidence of efficacy in treating RCSE. A major advantage is that ketamine may not require endotracheal intubation. In this study, we assess the safety and efficacy of ketamine in RCSE.

Methods: Since November 2009, we adopted a treatment protocol for treating RCSE including intravenous ketamine infusion. We administered two intravenous boluses of 2-3 mg/kg each of ketamine five minutes apart, immediately followed by continuous infusion of 10 mcg/kg/min. Based on clinical or electrographic responses, we increased dosage every 10 minutes or longer, using 2 to 10 mcg/kg/min increments, up to 60 mcg/kg/min. We also administered add-on Midazolam to prevent emergence reactions.

Results: Between November 2009 and December 2014, we treated with ketamine 18 RCSE episodes, obtaining a positive response in 13/18 (72%). Five children (age range: 2 months–7 years) with RCSE were treated with ketamine before using conventional anaesthetics, thus avoiding endotracheal intubation. Median dose of ketamine in continuum infusion was 30 mcg/kg/min (range 8-45). Median duration of ketamine administration was 2 days (range 1-5 days). An EEG pattern of burst-suppression was observed in all of them and resolution of RCSE after ketamine withdrawal persisted in 3/5 children. Minimal sialorrhea was the only adverse event observed.

Conclusions: Our series (Class IV of evidence) confirms the efficacy of ketamine in treating RCSE. Moreover, ketamine is well tolerated and does not require endotracheal intubation. It seems reasonable to use ketamine in RCSE prior to thiopental and propofol. Based on these encouraging results, we have designed a national multicentre randomised sequential trial, which has obtained the approval of the Italian Medicines Agency and is has now started in 10 paediatric emergency care centres nationwide.

P70

Monocentric prospective observational study of refractory/super-refractory status epilepticus: the experience of Modena

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Purpose: To evaluate the major clinical characteristics and outcomes of a prospective case series of adult patients presented with Refractory Status Epilepticus (RSE) or Super-Refractory Status Epilepticus (Super-RSE) (Shorvon et al. 2011) to NOCSAE Hospital, the hub center for neurological disorders of Modena district, northern Italy.

Material and methods: a mono-centric, prospective, observational study on consecutive patients with Refractory and Super-Refractory Status Epilepticus (RSE and Super-RSE) observed from 1 September 2013 and 31 August 2014. Data were collected using a specific "Status Epilepticus form". Outcome was evaluated at discharge and at 30 days, if data available.

Results: We observed 26 cases (age 16-93, average 67 years) of Refractory and Super-Refractory Status Epilepticus (31% of all 83 SE observed; 12 RSE, 14 Super-RSE). The majority was non-convulsive SE (N 17). Twenty patients presented an Acute Symptomatic SE (N 20) for which the most frequent causes were metabolic/sepsis and vascular etiologies in the RSE group, while almost all Super-RSE cases had post-anoxic etiology. Nineteen out of 26 cases presented with STESS (Rossetti et al. 2006) ≥ 3. Outcome: the SE was interrupted only in eight cases in the RSE and Super-RSE group (31%). A 30-days follow-up was available for 24 patients in the refractory group (92%): the mortality was 54% (13 patients) in the RSE/Super-RSE group compared to 22% in the responsive group (10 patients). The disability, measured by modified Rankin scale (mRs) at 30-days follow-up, showed that 96% of patients in the refractory group had mRs ≥3 or were dead.

Discussion and Conclusions: these preliminary data showed that RSE and Super-RSE are a quite common events (almost a third of all observed SE cases). Moreover these data confirms the high 1-month mortality and disability in RSE/super-RSE groups.

P71

Outcome of patients with refractory status epilepticus in Hong Kong

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Purpose: to review the outcome of patients with history of refractory status epilepticus in a tertiary hospital in Hong Kong

Method: retrospective chart review for cases who have history of refractory status epilepticus from Jan 2011 to Dec 2014. Patients' demographic data, clinical features, underlying diagnoses, treatment received and outcome were reviewed.

Results: Ten patients suffered from refractory status epilepticus during the study period. Their age ranged from four to eleven years old (7 boys and 3 girls). All except one had de novo onset of seizures. Two patients had prior developmental problems before the admissions for refractory status epilepticus. Majority of them had received more than one anesthetic agents (thiopentone or midazolam). Propofol was only used in two adolescent patients (16 and 17 years old respectively). The duration of intensive treatment ranged from 4 days to 6.5 months. Four patients n our cohort died and they usually died or deteriorated rapidly in the first 1-2 weeks. All survivors were complicated with active epilepsy after discharge from the intensive care unit. All except one were left with some degree of neuro-cognitive impairment.

Conclusion: Refractory status epilepticus is associated with high mortality, which is usually determined by underlying causes. Survivors are at high risk of developing active epilepsy and/ or neuro-cognitive impairment.

P72

Mortality after super-refractory status epilepticus in Finland

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Background: Status epilepticus (SE) is an important neurological emergency associated with significant mortality and morbidity. Status epilepticus is considered refractory (RSE) if the first and second line treatments with antiepileptic drugs fail and the patient needs to be treated with general anesthesia in the intensive care unit (ICU) and super-refractory (SRSE) if SE continues or recurs 24 hours or more after the onset of anesthetic therapy. Approximately12-43% all SE becomes refractory and 15 % super-refractory. The reported mortality rate of SRSE is between 30-50%.

Methods: We analysed retrospectively the Finnish Intensive Care Consortium Database in order to identify RSE and SRSE patients treated in ICU in Finland during a three-years-period (2010-2012). Data were available from all of Finland's five university hospitals and from 10 of the 15 central hospitals. The total referral population of these hospitals is 4,9 million. We included consecutive adult (16 years or older) RSE patients. Patients with hypoxic ischaemic brain damage and post-hypoxic myoclonus were excluded.

Results: We identified 395 patients with ICU-treated RSE and 87 (22 %) of them were classified as SRSE. This corresponds to annual incidence of SRSE 2/100 000. The median age was 57 years (range 17 - 84 years). The 1 – year mortality rate of SRSE was 37% and 23% in the RSE group.
Conclusions: Approximately 20% of all RSE patients treated in Finnish ICU´s are classified as super-refractory. The mortality rate of SRSE is the same as reported in earlier studies. SRSE seems to double the mortality rate of RSE.

P73

Analysis of refractory cases of generalized convulsive status epilepticus

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Objective: Analysis of cases of refractory generalized convulsive status epilepticus (GCSE).

Materials and Methods: The study involved 15 patients with GCSE (all women), aged from 21 to 62 years. GCSE was presented: as acute symptomatic (n=3 including subarachnoid hemorrhage -1, traumatic brain injury -2), in other cases - as a complication of epilepsy (n=12 including 9- symptomatic focal epilepsy, 3- cryptogenic one). Epileptiform activity (EEG) was localized: in frontal (n=4), in fronto-temporal (n=5), in the temporo-parietal (n=1). It was the hemispheric-lateralized in 2 cases and generalized in 3 cases. The provoking factors of GCSE were presented by combination of heredity to epilepsy and focal lesions of the brain (n=3), decompensation of somatic pathology (n=2), disruption of AEDs intake (missing doses/dose reduction n=3, independent abolition of AEDs intake n=3), iatrogenic (n=1). Super-refractory GCSE were verified in 7 cases. GCSE has been registered previously in 7 patients. Prehospital therapy included: intravenous diazepam (DZP) (n=6), valproic acid for intravenous use (VA) (n=3), the combination of DZP + VA (n=4). In 2 cases the GCSE has developed in the hospital, so intravenous antiepileptic drugs (AED) were not received during prehospital therapy. Initially, all patients received carbamazepine n=1, phenobarbital n=1, topiramate n=5, VA n=4, and levetiracetam (LEV) n=1; all patients with acute symptomatic GCSE did not receive AEDs previously. Methods of GCSE therapy were: addition of intravenous AEDs (benzodiazepines, VA, Lacosamid, LEV) and drugs for intravenous anesthesia (propofol, thiopental) to the AEDs base form during polytherapy.

Results: 2 patients (13.3%) with acute symptomatic status - died due to multiple organ failure not related to GCSE. In the remaining 13 cases, GCSE – was interrupted. Duration of the status were 3 - 120 hours. During treatment which included the usage of propofol in 6 patients and thiopental sodium in 2 patients, respiratory depression was noticed which obliged to the use of the ventilator and longer recovery.

Conclusions: The vast majority of refractory GCSE - in adults (46.6%) was provoked by disruption of – AEDs intake. Refractory cases of GCSE were observed mainly in symptomatic focal (frontal, fronto-temporal) epilepsy (60%). The death was noticed only in cases of acute symptomatic GCSE.

P74

Seven cases of new onset refractory status epilepticus (NORSE) syndrome: outcomes with early immunotherapy

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Cryptogenic new onset refractory status epilepticus (NORSE) syndrome has been described in both adults and children, and is often associated with poor outcome. A variety of terms have been used in the literature to refer to this syndrome. The condition may be triggered by as yet unidentified infections or an immunological mechanism. We present a series of 7 patients with NORSE syndrome trea-

ted at Hamad Medical Corporation in Qatar, in whom early use of immunotherapy appears to be associated with good neurological outcome.

Methods: Case note review of the index case and six other patients was undertaken to obtain details of clinical presentation, imaging and CSF findings, infectious/inflammatory tests, management of seizures, immunotherapy and outcome.

Results: Previously healthy 45-year-old right-handed man presented with episode of abnormal behavior and confusion on the background of 3-days history of fever, malaise. EEG showed evidence of continuous subclinical partial seizure. He was loaded with intravenous Phenytoin. The next day after admission patient developed status of generalized tonic-clonic seizures. He was intubated for airway protection, started on Midazolam followed by Propofol IV infusion and placed on continuous EEG monitoring. He continued to have electrographical seizures, despite multiple anticonvulsant medications, including high doses of Levetiracetam, Valproic acid, Topiramate, Phenytoin, Phentobarbitone. Seizures recurred on withdrawal of barbiturate anesthesia until day 29. CSF examination and serological tests for viral and autoimmune etiologies were normal. At the onset of status epilepticus, the MRI showed bilateral temporal increased T2 and FLAIR signal intensity. Subsequent MRI studies performed 1 month later demonstrated bilateral hippocampal atrophy and mild increased bitemporal T2 signal intensity. He was initially treated with acyclovir and antibiotics. IV immunoglobulin was administered in day 20 with good recovery being transferred to Rehab with mild neurological deficit. Clinical features and investigations of the six other patients were similar. Five patients were given early immunotherapy with steroids and intravenous immunoglobulins. Three of them improved completely without neurological deficit, another two, survived with moderate degree of neurological deficit. Two patients who were not given immunotherapy died from complications associated with prolonged ICU stay.

Conclusion: In our experience, early immunotherapy has been associated with good outcomes in NORSE. Based on clinical data of our patient and those described in the literature, we characterized the NORSE syndrome. Multicentre collaboration is required to establish the diagnostic criteria and appropriate management of patients presenting with NORSE.

P75

In quest of a reduction in mortality and a consensus for the management of super-refractory status epilepticus

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Super-refractory status epilepticus has a high mortality and morbidity. Relapse may occur on repeated weaning attempts of anaesthetic agents (principally propofol, midazolam, thiopental), despite concomitant use of antiepileptic drugs such as levetiracetam, phenytoin, phenobarbital, lacosamide, valproate and topiramate. Surgical resection is only applicable in a minority. In new onset refractory status epilepticus, treatments (steroid, plasma exchange and IVIG) for a presumed immune-mediated process are often administered and treating a proven or postulated underlying cause is an essential part of management.

In our experience, thiopental is often the most effective agent but, particularly with prolonged use, it is toxic with an unfavourable adverse effect profile including infection, multi-organ dysfunction, cardiomyopathy, haemodynamic instability, acidosis and gut stasis, and is likely to significantly contribute to a fatal outcome. Therefore, other treatments, for which there is limited evidence, but which, nevertheless, might reduce thiopental use are needed until remission. Choice of treatment at this stage depends on availability and local experience. Small numbers and cost make large multicentre randomised trials difficult to set up but this should not be a bar to proposing a pathway aimed at facilitating timely and coherent interventions across units, allowing prospective, multicentre outcome audits as previously suggested[1]. In the absence of randomised trials we propose a pathway based on likely efficacy versus least harm. The 2015 Colloquium can provide a forum for discussion for the proposed pathway.

If weaning of an anaesthetic agent is unsuccessful after burst suppression for three days, we suggest in order of use: corticosteroids, ketamine, high dose intravenous magnesium, mild hypothermia and ketogenic diet through the enteral route (if gut stasis does not preclude this). If the above are unsuccessful, stimulation modalities can be considered if available. In ongoing refractory generalised status epilepticus, deep brain stimulation could be then considered. In focal status, external trigeminal and vagus nerve stimulation, magnetic stimulation, and focal stimulation may all be considered, with non-invasive modalities applied earlier.

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P76

Claustrum damage and refractory status epilepticus following febrile illness

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Objective: to characterize the clinical, EEG, and brain imaging findings in an adult case-series of patients with de novo refractory status epilepticus (SE) occurring after a febrile illness.

Methods: a retrospective study (2010-2013) was undertaken with the following inclusion criteria: (a) previously healthy adult (> 16 years of age) with refractory SE; (b) onset of seizures 0–21 days after a febrile illness, and (c) lacking evidence of infectious agents in CSF; (d) no previous history of seizures (febrile or afebrile), as well as previous or concomitant neurological disorder. Among 185 refractory SE cases observed in the study period, five (21 – 35 years-old) fulfilled the inclusion criteria.

Results: confusion and stupor were the most common symptoms at disease onset, followed after a few days by acute repetitive seizures that were uncountable in all patients. Seizures consisted of focal motor/myoclonic events with alternating side involvement and secondarily generalization. Anti-epileptic drugs failed in every patient to control seizures; all subjects requiring intensive care unit admission. Barbiturate-coma with burst-suppression pattern was applied in three out five patients for 5 – 14 days. One subjects died in the acute phase. In each patient we observed a reversible bilateral hyperintensity of the Claustrum time-related with SE. All patients showed negative results on multiple neural antibodies testing (including VGKC, VGCC, NMDAR, AMPAR). Chronic epilepsy was present in the three out of four that survived.

Conclusions: we described a group of adult patients with febrile-infection related status epilepticus sharing many analogies with the FIRES syndrome observed in children and we outlined the role of Claustrum damage in this condition. Future prospective studies are needed to delineate the specificity of this imaging biomarker, its pathogenetic role in refractory status epilepticus, and finally the aetiology of the condition.

P77

Pyridoxine deficiency in adult status epilepticus patients

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Background: A case of an 8 year old girl we treated for super-refractory status epilepticus (SRSE) was found to

have a low pyridoxine level at 5 ug/L. Improvement in the EEG was seen after pyridoxine was given. We decided to look at the pyridoxine levels in adult patients admitted with status epilepticus.

Methods: With IRB approval, we reviewed records of patients admitted for status epilepticus from January 2014 to January 2015. 60 adult patients were identified with documented pyridoxine levels. For comparison purposes, we looked at pyridoxine levels in Epilepsy outpatients from the past three years. Reported normal pyridoxine range is 5 to 50 ug/L.

Results: All but four patients had low normal or undetectable pyridoxine levels. Of 143 adult outpatients only 39% had a low normal pyridoxine level and none were undetectable. The mean pyridoxine was 5.5 ug/L in the status group and 25.2 ug/L in the outpatient group (statistically significant ($p<0.0001$ using Fisher's exact test). B1, B2 and B12 vitamin deficiencies were not seen in the status group.

Discussion: Pyridoxine is a water-soluble vitamin that is naturally present in many foods. The active component, pyridoxal 5' phosphate (PLP), binds to intracerebral glutamic acid decarboxylase(GAD) which is the enzyme responsible for the conversion of glutamate to GABA. Without PLP, GABA cannot be synthesized and glutamate remains elevated in the synapse thereby increasing neuronal excitability. GABA deficiency is seen in pyridoxine dependent genetic epilepsy. A number of factors can lower pyridoxine levels including malabsorption, inflammation, kidney disease alcohol dependence, pregnancy, obesity and antiepileptics (valproic acid, dilantin, carbamazepine).

Conclusions: GABA is important in seizure suppression, and PLP is crucial for GABA synthesis. Low levels of pyridoxine may make individuals more susceptible to seizure activity and super-refractory status. In status patients, pyridoxine deficiency was found in 65.6% (compared to 10.6% in the outpatients) and very low levels were present in 27.1% which leads us to believe that there is a relationship between status epilepticus and pyridoxine levels.

P78

Cryptogenic new onset refractory status epilepticus: case report

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Background: Refractory status epilepticus is a severe condition in which seizures do not respond to the first and second line of anticonvulsants. Sometimes it appears suddenly, in patients with no history of epilepsy. This is referred "new onset refractory status epilepticus" (NORSE). In most cases, the identification of viral agents is performed. However, in some patients, the aetiology cannot be identified despite a thorough investigation. These cases are called "cryptogenic". We report a patient with no history of epilepsy, who presented a cryptogenic NORSE.

Methods: A 22-year old woman with no history of epilepsy or other important medical disease was admitted due to continuous tonic- clonic seizures without recovery in between. She was treated with i.v. Lorazepam (0.1 mg / kg) and i.v. phenytoin 20 mg / kg and she was intubated. Despite this treatment, she continued with clinical seizures. The EEG showed generalized continuous epileptiform activity. A continuous infusion of midazolam was performed until a burst- suppression pattern was observed.MRI within 24 hours of onset, showed increased T2 signal in both hippocampi. CSF: mild lymphocytic pleocytosis, normal glucose and slight elevation of proteins. Screening: HSV I, II HSV, VZV, EBV, HHV 6, HIV, VDRL, CMV, JC: negative. Toxicological screening: negative. ANA, anti-thyroid antibodies, anti-dsDNA, ANCA, Jo-1, Ro, La, Rheumatoid factor, ESR, C-reactive protein, serum ACE level, anti tTG, anti-endomysium, CSF immunoelectrophoresis: negative. CT thorax, abdomen, pelvis, gynaecological ultrasound, whole body PET, CSF cytology : negative. Serum and CSF lactate: Normal. Anti Yo, Anti-Hu, Anti Ri, Anti NMDAR, AMPAR, GABAbR, LGI 1, Caspr 2, GABAaR: negative. Results: Screening for neoplasias or autoimmune encephalitis antibodies: negative. NORSE duration was 31 days. Patient recovered with sever epilepsy and cognitive impairment.

Conclusion: NORSE is a diagnosis of exclusion, and should be done after paraneoplastic or infectious causes have been ruled out.

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P79

Historical note on a fatal status epilepticus documented at Salzburg in 1617

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Background: Wolf Dietrich of Raitenau ruled the archiepiscopal Salzburg from March 2nd 1587 to December 17th 1611. He was condemned by his successor Markus Sittikus to spend his last years imprisoned at the burg Hohensalzburg, where he died on January 16th 1617.

Methods: The original Latin handwriting, including the anamnesis and the autopsy of the archbishop´s body performed by his personal physician, were analysed in synopsis with historical handwritings of St. Peter´s abbey, Salzburg and Archbishop Markus Sittikus.

Results: Wolf Dietrich had his first well documented stroke in winter 1604/05. He had a palsy of his right arm, was unable to write and used a stamp instead of his signature until October 1605.
After another right hemispheric stroke with persisting palsy of his left arm ["leva corporis pars iam pridem simili ex apoplectico assultu in paralysin resoluta"], he developed symptomatic epilepsy with recurring seizures ["epileptico insultu quo etiam alias correptus est"].
On January 15th 1617 he suffered from a secondarily generalized convulsive status epilepticus ["toto corpore convellitur epileptico insultu"] with stertorous breathing, distortion of his face ["spuma stertore insigni faciei perversione"] and was unconsciousness for eight hours. He recovered from coma and showed dysphagia, buccofacial apraxia ["abolitam diglutiendi facultatem"] reversible aphasia or speech arrest ["accisa etiam verba loqui"] and left sided hemiplegia ["leva corporis pars... immobilis prorsus est reddita"]. The following day, speech disturbances impaired and he died at noon.
His autopsy showed large but sane liver ["hepar magnum sanum"] and heart ["cor magnum in quo lapsus nullus"], a former lung fissure, intrapulmonal mucus ["pituita imbutus"], five kidney stones and a partly cirrhotic spleen. The cause of his death was assumed to be intracerebral ["causa mortis in capite requienda fuisset"].

Conclusion: Wolf Dietrich´s suffering is the first witnessed case report on fatal status epilepticus in Salzburg.
Most likely, he suffered from vascular epilepsy due to a former right hemispheric stroke, leading to status epilepticus with left sided Todd´s palsy and speech disturbances. An acute symptomatic aetiology of the status cannot be ruled out strictly, as for religious reasons the archbishop´s brain was not autopsied.

P80

EpiNet database used for observational study of status epilepticus in Auckland, New Zealand

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Background: The EpiNet project has been established to facilitate clinical research in epilepsy (www.epinet.co.nz). The database can be accessed from anywhere in the world by approved investigators via a secure, password-protected website. Information is collected according to multiple axes: epilepsy overview; seizure history; electroclinical syndrome; aetiology; investigations; drug treatment.
The EpiNet database has been adapted to collect detailed information on patients with status epilepticus (SE). It is being used for an epidemiological study of SE in Auckland, and is being developed to enable multicentre clinical trials.

Methods: A prospective, incidence study of SE is being conducted in the greater Auckland area (population 1.5 million), commencing March 2015. Information will be systematically collected over the next year on all patients over 4 weeks of age who have a seizure of more than 10 minutes duration (definition of SE for this study). Patients will be followed for 2 years.
New forms have been created in EpiNet to record detailed information regarding SE. The new ILAE classification system for SE is being used. The time base for recording information within EpiNet has been expanded to precisely record time of onset and duration of SE. The time and route (IV, IM, oral, nasogastric, buccal, nasal, rectal) of administration of various treatments - conventional anti-epileptic drugs and other treatments (e.g. anaesthetic agents, steroids, other immunosuppressive drug treatment, intravenous immunoglobulin, plasma-exchange, ventilation, cooling, diet) - is being recorded in a similar manner.

Results: Descriptive statistics will be provided on demographic and clinical variables, and the incidence of SE in Auckland (per 100,000 person years with 95%CI) will be determined. The adjusted hazard ratio will be calculated for possible prognostic factors (age, sex, ethnic group, seizure type, aetiology, and duration).
Exploratory analyses will determine associations between: the presence of any treatment effect; time to stop SE; global outcome (Modified Rankin score); cumulative mortality and time-dependent risk of epilepsy during 2 years of follow-up.

Conclusions: The incidence, causes, responses to treatment, and outcomes of SE in Greater Auckland will be determined.
The EpiNet database is being developed for multi-centre randomised controlled trials in SE.

P81

How much does it cost to identify a critically ill child experiencing electrographic seizures?

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Background: Electrographic seizures in critically ill children may be identified by continuous electroencephalographic (EEG) monitoring. We evaluated the cost-effectiveness of four electrographic seizure identification strategies (no EEG monitoring and EEG monitoring for 1 hour, 24 hours, or 48 hours).

Methods: We created a decision tree to model the relationships among variables from a societal perspective. To provide input for the model, we estimated variable costs directly related to EEG monitoring from their component parts, and we reviewed the literature to estimate the probabilities of outcomes. We calculated incremental cost-effectiveness ratios to identify the tradeoff between cost and effectiveness at different willingness-to-pay values.

Results: Our analysis found that the preferred strategy was EEG monitoring for 1 hour, 24 hours, and 48 hours if the decision maker was willing to pay <$1,666, $1,666-$22,648, and >$22,648 per critically ill child identified with electrographic seizures, respectively. The 48 hour strategy only identified 4% more children with electrographic seizures at substantially higher cost. Sensitivity analyses found that all three strategies were acceptable at lower willingness-to-pay values when children with higher electrographic seizure risk were monitored.

Conclusions: Our results support monitoring of critically ill children for 24 hours because the cost to identify a critically ill child with electrographic seizures is modest. Further study is needed to predict better which children may benefit from 48 hours of EEG monitoring since the costs are much higher.

P82

Google search behavior for status epilepticus

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Background: Millions of people surf the Internet every day as a source of health care information looking for materials about symptoms, diagnosis, treatments and their possible adverse effects, or diagnostic procedures. Google is the most popular search engine and is used by patients and physicians to search for online health-related information. This study aimed to evaluate changes in Google search behavior occurring in English-speaking countries over time for the term "status epilepticus" (SE).

Methods: Using Google Trends, data on global search queries for the term SE between 1st January 2004 and 31th December 2014 were analyzed. Search volume numbers over time (downloaded as CSV dataset) were analyzed by applying the "health" category filter.

Results: The research trends for the term SE remained fairly constant over time. The greatest search volume for the term SE was reported in the United States, followed by India, Australia, the United Kingdom, Canada, the Netherlands, Thailand, and Germany. Most terms associated with the search queries were related to SE definition, symptoms, subtypes and treatment. The volume of searches for some queries (non-convulsive, focal, and refractory SE; SE definition; SE guidelines; SE symptoms; SE management; SE treatment) was enormously increased over time (search popularity has exceeded a 5000% growth since 2004).

Conclusions: Most people use search engines to look for the term SE to obtain information on its definition, subtypes, and management. The greatest search volume occurred not only in developed, but also in developing countries, where raising awareness about epilepsy still remains a challenging task and where there is reduced public knowledge of epilepsy.
Health information seeking (the extent to which people search for health information online) reflects the health-related informative needs of Internet users for a specific disease. Google Trends shows that Internet-users have a great demand of information concerning some aspects of SE (definition, subtypes, symptoms, treatment and guidelines). Policy makers and neurological scientific societies have the responsibility to try to meet these informative needs and to better target public informative campaigns on SE to the general population.

P83

Status epilepticus leads to inflammation in the eyes

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Epileptic seizures are known to cause extensive immune response in the brain. However, it is not known whether this inflammatory response can spread to areas outside cortical/subcortical structures. In order to investigate this, we set out to study the immune response in eyes following status epilepticus (SE). Adult rats underwent electrically-induced temporal status epilepticus and eyes were studied acute (6hrs), sub-acute (1w) and late (7w) after seizures. Our data show that levels of cytokines and chemokines at

6hrs following SE are not altered in the eyes, compared to non- stimulated controls (NSC). The cytoarchitecture of the retina appeared normal at 1w and there were no differences in numbers or morphology of microglial cells. However, at 7w we saw an increase in number of retinal microglia, both ipsi- and contralateral to the epileptic foci. Interestingly, they remained located within the plexiform layers, but often in clusters and with more processes in the outer nuclear layer of the retina. Percentage of ramified microglia was also decreased, while amoeboid morphology was increased. We detected no changes in numbers of phagocytic cells, infiltrating macrophages, or vascular pericytes. In addition to microglial changes, we observed a shift in Müller cell and astrocyte activation, showing more and longer processes compared NSC. In line with microglial activation, seizure –induced synaptic changes were observed in the outer nuclear layer, attributed to a reduction in the post-synaptic density -95 protein. These results are the first evidence that epileptic seizures induce an immune response in the eyes and may be used as a novel less invasive diagnostic tool to study brain inflammation.

P84

Clinical validation study of the Salzburg consensus criteria for diagnosis of non-convulsive status epilepticus (SCNC)

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Objective: Consensus criteria (SCNC) for diagnosis of non-convulsive status epilepticus (NCSE) were discussed at the 4th London-Innsbruck Colloquium on Status epilepticus in Salzburg 2013 and published recently. The aim of this multi-center study is the clinical validation of SCNC.

Methods: EEGs of patients with referral diagnosis of "clinical suspicion of NCSE" were identified and evaluated for: (1) more than 25 epileptiform discharges (ED) per 10 s epoch; (2) patients with EDs 2.5/s or less or rhythmic delta/theta-activity exceeding 0.5 /s AND at least one of (2a) clinical and EEG-improvement to antiepileptic drugs, (2b) subtle clinical phenomena, or (2c) typical spatiotemporal evolution. In case of fluctuation without evolution, or EEG without clinical improvement, "possible NCSE" was diagnosed. The criteria followed the rules of the latest publication of the American Clinical Neurophysiology Society. EEG recordings from 66 consecutive patients (33 patients from Salzburg, 25 patients from Dianalund and 8 patients from Aarhus) were retrospectively scored according to the SCNC. The gold standard was the final clinical diagnosis extracted from the medical charts.

Results: the sensitivity of SCNS was 96.2 %, specificity 62.5 %, and accuracy 75.8 %. NCSE was diagnosed based on (1) in 22.7 %, (2a) in 7.6 %, (2b) in 13.6 %, and (2c) in 4.5 %. "Possible NCSE" based on fluctuation without evolution in 13.6 %. "NCSE in coma" was found in 6.1 %, pre-existing epilepsy in 59.1 % of the patients.

Conclusion: SCNC are a clinically useful tool, with high sensitivity. Yet the specificity needs further improvement. Based on our data a modified version of the SCNC is to be tested in a prospective study.

P85

Retrospective evaluation of Salzburg Consensus Criteria for diagnosis of Non-Convulsive status epilepticus (SCNC)

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Objective: Consensus criteria (SCNC) for diagnosis of non-convulsive status epilepticus (NCSE) were discussed at the 4th London-Innsbruck Colloquium on Status epilepticus in Salzburg 2013 and published recently. The aim of this multi-center study is the retrospective validation of SCNC in a sample of definite NCSE.

Methods: the EEGs of patients with NCSE were investigated for morphological characteristics in each of two epilepsy centres, i.e. Danish Epilepsy Centre (Dianalund, Denmark) and Dep. of Neurology, CDK, Paracelsus Medical University (Salzburg, Austria).

Results: Reported are the preliminary results of 56 consecutive patients identified by discharge diagnosis of NCSE from January to June 2014 in Salzburg. Various EEG-patterns used for diagnosis according the SCNC for "NCSE" were found: spatiotemporal evolution in 25 %, subtle clinical ictal phenomenon in 14.3 %, frequency of epileptiform discharges (ED) ≥2,5 Hz: 3,6 %, EEG- and clinical response to AED: 0 %. For "possible NCSE": Fluctuation without evolution 50 %, EEG- without clinical response to AED 7.1 %. A rate of ED ≥2 Hz was detected in 11 %. In order to find false positives, a second population of 100 consecutive EEGs of patients without NCSE was investigated. Fluctuation without evolution exceeding 10 consecutive seconds was found in 35 % of EEGs, whereas spatiotemporal evolution and ED ≥2,5 Hz were not found.

Conclusion: SCNC are a clinically useful tool, yet need to be investigated in prospective trials. Only minor amendments are recommended.

P86

Burden of illness for super refractory status epilepticus patients

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Objective: To provide an accurate estimate of the annual number of super-refractory status epilepticus (SE) cases in the US and to evaluate the hospital healthcare costs and charges associated with treating this condition.

Methods: This was a cross-sectional study that utilized the Premier Hospital database to estimate the number of super-refractory SE hospital discharges during 2012. The number of hospitalizations was projected to estimate the total number of super-refractory SE hospitalizations in the US. Length of stay (LOS) in hospital, days spent in the Intensive Care Unit (ICU), hospital costs and healthcare provider charges were also analyzed.

Results: A total of 36.8 million discharges were included in the Premier Hospital database for 2012. A total of 6,325 super-refractory SE hospital discharges were identified in the dataset, which projected to 41,156 cases of super-refractory SE throughout the US in 2012. The mean LOS was 16.5 days (SD: 24.3) and the mean number of days spent in ICU was 9.3 (SD:10.9). The mean cost of treatment was $51,247 (range: $14,700 to $156,500) and the mean charge was $189,115 (range: $51,800 to $459,000).

Interpretation: Super-refractory SE hospitalizations are long, intense and place a high burden on healthcare resources. The projected number of national super-refractory SE cases was higher than estimations based on previous reports. These data indicate that super-refractory SE may be under-diagnosed and continues to be area of high unmet medical need.

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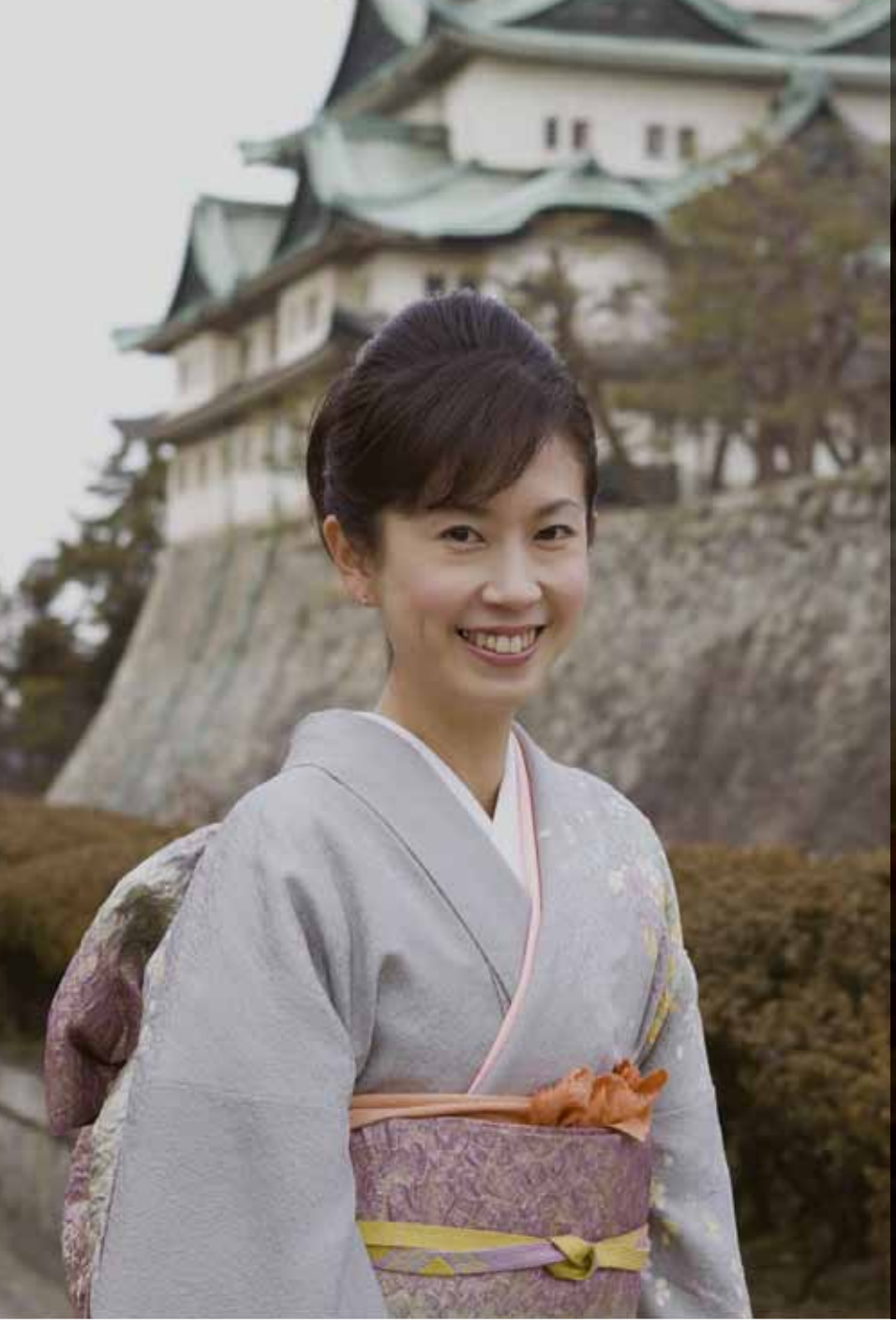
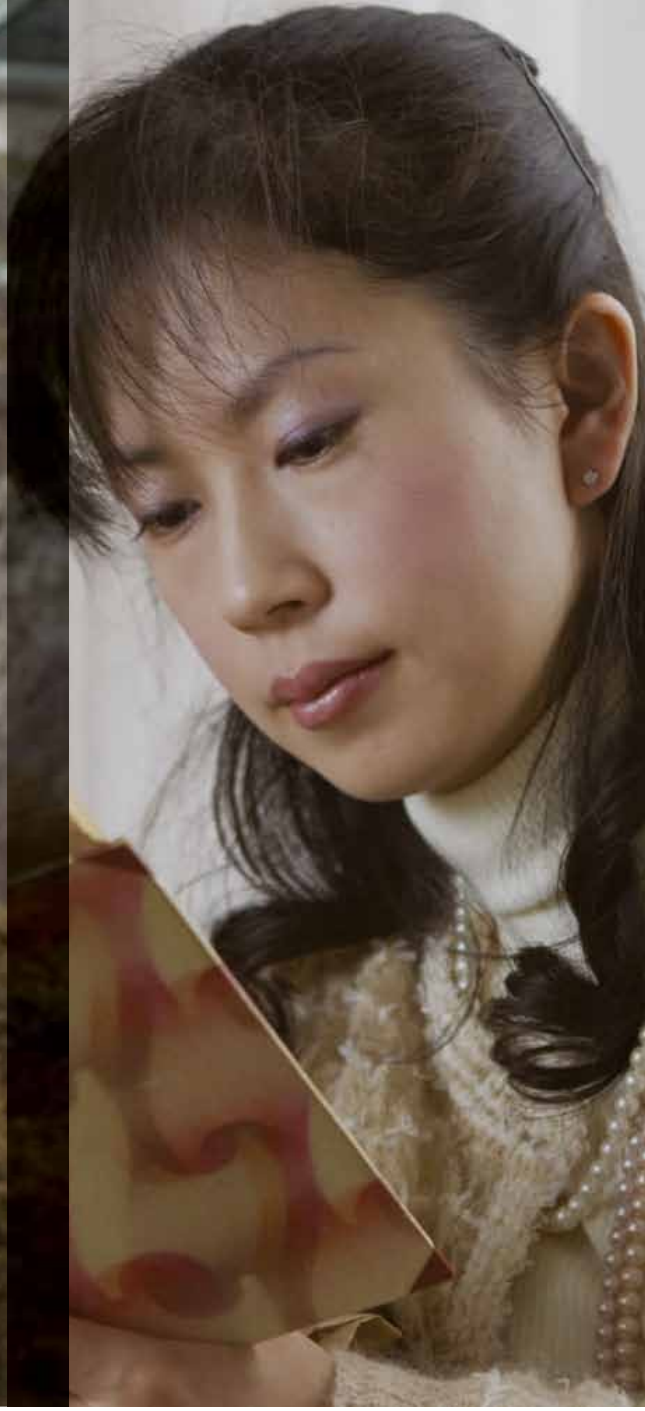
of the institutions and companies listed below:





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