The 6th London-Innsbruck Colloquium on Status Epilepticus and Acute Seizures
6-8 April 2017
Salzburg, Austria

Final Programme

www.statusepilepticus.eu
**PATRONS**

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**CHAIRS**

Eugen Trinka, Salzburg, Austria  
Simon Shorvon, London, United Kingdom
Dear friends and colleagues,

It is our sincere pleasure to welcome you all once again to Salzburg as the venue for the 6th London-Innsbruck Colloquium. The previous colloquia (London 2007, Innsbruck 2009, Oxford 2011, Salzburg 2013 and London 2015) were highly successful, and these biannual colloquia have become a popular feature of the international epilepsy calendar. This conference will focus on current basic and clinical research in status epilepticus, clinical aspects and new therapies – with the aim of stimulating thought and discussion and improving treatment and outcome of this condition.

It is our intention over the 3 days of the conference to have intensive and interactive discussions on the cutting edge of research and clinical practice in the field of Status Epilepticus. We have deliberately left space in the programme for the audience to question and 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.

In addition we have arranged a Colloquium Dinner at the Kavalierhaus Klessheim and look forward to a nice evening with all of you. Salzburg is capital to the province of the same name, and it is home to 150,000 inhabitants. We hope you also have time to explore the charming town which is the birthplace of Mozart, and visit its historic city centre and the many interesting and historical sites.

With very best regards

Eugen Trinka and Simon Shorvon
Co-Chairs, 6th London-Innsbruck Colloquium on Status Epilepticus and Actue Seizures
Information for Speakers & Poster Presenters

Information for speakers

Please make sure to bring your PowerPoint presentation on a USB-stick to the MEDIA CHECK at the congress centre 2 hours prior to the start of your session at the very latest. Do not bring your own laptop for the presentation. Standard format will be 4:3, but 16:9 is also possible. In case your presentation contains video sequences, please ensure to bring them with you and pack them with a standard codec. 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.

Disclosure of potential conflicts of interest

Speakers at the 6th London-Innsbruck Colloquium on Status Epilepticus and Acute Seizures are requested to disclose their potential conflicts of interest. Consequently, a conflict of interest statement should be included on your first slide.

Information for poster presenters

POSTER FORMAT:
Please bring your poster in portrait style. The measures should not exceed 90cm in width and 150cm in height. Mounting material will be provided on site. All posters should be displayed during the entire Colloquium and mounted on Thursday, April 6 in the morning. They have to be taken down on Saturday, April 8 by the end of the Colloquium. If you do not remember your poster board number, please look it up in the list of posters on page 19.

POSTER DISCUSSION:
There will be two sessions explicitly dedicated to the posters. The dates and times are scheduled as follows:

- Thursday, April 6: 12.45 - 13.15
- Friday, April 7: 13.00 - 14.00

During these two sessions, you or one of your co-authors must be at your poster site and be prepared to answer questions.

POSTER AWARDS
Three poster prizes will be awarded in the following categories:
- Basic and clinical investigations
- Paediatric and clinical science
- Treatment and outcome
The prizes will be officially awarded on Friday, April 7, 16.30-17.00.
THURSDAY APRIL 6TH 2017

08.30 - 08.45  ILAE address and opening of the conference
E. Perucca (Italy), E. Trinka (Austria), S. Shorvon (UK)

08.45 - 10.45  The nature of status epilepticus: experimental aspects I
D. Kullman (UK), H. Cock (UK)

08.45 - 09.05  Mitochondrial diseases and status epilepticus
S. Rahman (UK)

09.05 - 09.25  Discussion

09.25 - 09.45  Circuit mechanisms in status epilepticus
J. Kapur (USA)

09.45 - 10.05  Discussion

10.05 - 10.25  Receptor trafficking
J. Kittler (UK)

10.25 - 10.45  Discussion

10.45 - 11.15  Break

11.15 - 12.45  The nature of status epilepticus: experimental aspects II
M. Rogawski (USA), M. Walker (UK)

11.15 - 11.35  Epigenetic changes in status epilepticus
D. Henshall (Ireland)

11.35 - 11.55  Discussion

11.55 - 12.25  Neurotrophic factors and status epilepticus
M. Simonato (Italy)

12.25 - 12.45  Discussion

12.45 - 13.15  Break and poster viewing

13.15 - 14.15  Industry sponsored symposium and lunch
(for details see page 80)
<table>
<thead>
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<th>Time</th>
<th>Session</th>
<th>Speaker</th>
<th>Country</th>
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</thead>
<tbody>
<tr>
<td>14.15 - 15.15</td>
<td>The nature of status epilepticus: clinical aspects I</td>
<td>R. Kälviäinen (Finland), G. Bauer (Austria)</td>
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<td>14.15 - 14.35</td>
<td>Next generation sequencing in the diagnosis of encephalitis</td>
<td>W. I. Lipkin (USA)</td>
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<td>14.35 - 14.55</td>
<td>Discussion</td>
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<td>Boundary syndromes</td>
<td>S. Shorvon (UK)</td>
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<td>15.15 - 15.35</td>
<td>Discussion</td>
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<td>15.35 - 15.55</td>
<td>Status epilepticus due to poisons in warfare</td>
<td>A. M. Marini (USA)</td>
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<td>15.55 - 16.15</td>
<td>Discussion</td>
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<td>16.15 - 16.45</td>
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<td>16.45 - 18.05</td>
<td>The nature of status epilepticus: clinical aspects II</td>
<td>A. Neligan (UK), I. Unterberger (Austria)</td>
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<td>16.45 - 17.05</td>
<td>Neuroimaging of status epilepticus</td>
<td>S. Meletti (Italy)</td>
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<td>17.05 - 17.25</td>
<td>Discussion</td>
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<td>17.25 - 17.45</td>
<td>Treatment gap in developing countries</td>
<td>B. Lee (South Korea)</td>
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<td>17.45 - 18.05</td>
<td>Discussion</td>
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<td>Colloquium Dinner</td>
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<td>08:30 - 10:30</td>
<td><strong>Status epilepticus in the Intensive Care Unit I</strong></td>
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<td>N. Abend (USA), P. Kaplan (USA)</td>
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<td>08.30 - 08.50</td>
<td><strong>NCSE – types and EEG</strong></td>
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<td>E. Trinka (Austria)</td>
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<td>08.50 - 09.10</td>
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<td><strong>Prognostic scales in status epilepticus</strong></td>
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<td>F. Yuan (China)</td>
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<td><strong>Anaesthetic treatment of status epilepticus</strong></td>
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<td>S. Hocker (USA)</td>
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<td>10.10 - 10.30</td>
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<td>11.00 - 11.20</td>
<td><strong>Status epilepticus in the Intensive Care Unit and the weaning of anaesthetics</strong></td>
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<td>T. Bleck (USA), M. Leitinger (Salzburg, Austria)</td>
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<td>11.00 - 11.20</td>
<td><strong>Guidelines for the weaning of anaesthetics</strong></td>
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<td>H. Colquhoun (USA)</td>
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<td>11.20 - 11.40</td>
<td><strong>Anaesthetic effects on the EEG: Implications for the management of Super Refractory Status Epilepticus</strong></td>
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<td>A. Cole (USA)</td>
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<td>11.40 - 12.00</td>
<td><strong>Discussion on the topic of weaning anaesthetics</strong></td>
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<td>12.00 - 12.20</td>
<td><strong>Long term consequences of intensive care treatments</strong></td>
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<td>T. Loddenkemper (USA)</td>
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<td>12.20 - 12.40</td>
<td><strong>Status epilepticus in the elderly</strong></td>
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<td>I. Leppik (USA)</td>
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<td>13.00 - 14.00</td>
<td>Lunch and poster viewing</td>
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<td>14.00 - 15.00</td>
<td><strong>Some regulatory aspects of status epilepticus</strong></td>
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<td><strong>Is status epilepticus an entity?</strong></td>
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<td>S. Shorvon (UK)</td>
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<td>14.20 - 14.40</td>
<td><strong>What evidence do we need to license a drug for status epilepticus?</strong></td>
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<td>E. Trinka (Austria)</td>
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<td><strong>Discussion</strong></td>
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<td><strong>Audits and registries</strong></td>
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<td>S. Basic (Croatia), A. Strzelczyk (Germany)</td>
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<td>15.30 - 15.50</td>
<td><strong>The global audit of refractory status epilepticus</strong></td>
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<td>S. Hocker (USA) and M. Ferlisi (Italy)</td>
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<td><strong>Discussion</strong></td>
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<td><strong>SENSE registry for status epilepticus</strong></td>
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<td>C. Kellinghaus (Germany)</td>
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<td><strong>Discussion</strong></td>
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<td><strong>Poster award</strong></td>
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<td>17.00 - 17.30</td>
<td><strong>Group photo</strong></td>
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SATURDAY APRIL 8TH 2017

08.30 - 10.00  Future perspectives, novel therapy and innovation I
S. Hocker (USA), A. Rossetti (Switzerland)

08.30 - 08.50  Propofol Hemisuccinate
M. Rogawski (USA)
08.50 - 09.00  Discussion

09.00 - 09.20  Valnoctamide and SPD for acute seizures and status epilepticus
M. Bialer (Israel)
09.20 - 09.30  Discussion

09.30 - 09.50  Brivaracetam
E. Trinka (Austria)
09.50 - 10.00  Discussion

10.00 - 10.30  Break

10.30 - 14.30  Future perspectives, novel therapy and innovation II
N. Bharucha (India), S. Ruegg (Switzerland)

10.30 - 10.50  Perampanel – an oral AMPA antagonist
A. Rohracher (Austria)
10.50 - 11.00  Discussion

11.00 - 11.20  Place of neurosteroids in the treatment of status epilepticus
A. Rossetti (Switzerland)
11.20 - 11.30  Discussion

11.30 - 11.50  Ketamine
J. Höfler (Austria)
11.50 - 12.00  Discussion

12.00 - 12.30  Break
12.30 - 12.50  New modes of administration  
J. Cloyd (USA)

12.50 - 13.00  Discussion

13.00 - 13.20  Canine status epilepticus – implications for humans  
W. Löscher (Germany)

13.20 - 13.30  Discussion

13.30 - 13.50  Reactive Oxygen Species in status epilepticus  
M. Walker (UK)

13.50 - 14.00  Discussion

14.00 - 14.20  Update ESET Trial  
J. Kapur (USA)

14.20 - 14.30  Discussion

14.30 - 14.45  Concluding remarks  
S. Shorvon (UK), E. Trinka (Austria)

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**BASIC SCIENCE**

**P01**
Diurnal circulating microRNAs profiles in canines with naturally occurring epilepsy
Bridget Curtin (Minneapolis, United States)

**P02**
Developmental changes of adenosinergic system in hippocampal excitability after status epilepticus in immature and adult rats
Petr Fabera (Prague 5, Czech Republic)

**P03**
Differentially expressed long non-coding RNAs in the brain of pilocarpine-induced mouse epilepsy model
Yoonhyuk Jang (Seoul, South Korea)

**P04**
Procalcitonin: dynamic changes and function research in status epilepticus
Yue Ma (Xi’an, China)

**P05**
Closed-loop gene therapy for intractable focal epilepsy
Andreas Lieb (London, United Kingdom)

**P06**
Action of adenosine A1 agonist on cortical epileptic afterdischarges is modified after status epilepticus in immature rats
Pavel Mares (Prague, Czech Republic)

**P07**
Assessment of anti-seizure and neuroprotective effects of phenobarbital and memantine in a delayed-treatment rat model of organophosphate exposure
F. Edward Dudek (Lake City, United States)

**P08 – BEST POSTER**
Inhibition of monoacylglycerol lipase (MAGL) by CPD-4645 protects mice against refractory status epilepticus (SE) and its therapeutic effects are potentiated by the ketogenic diet
Gaetano Terrone (Milan, Italy)
**P09 – BEST POSTER**
Long-term epilepsy after post stroke status epilepticus (PSSE)
Laura Abraira (Barcelona, Spain)

**P10**
Status epilepticus after cardiac arrest - electrographic characterisation of the ictal-interictal continuum
Sofia Backman (Lund, Sweden)

**P11 – BEST POSTER**
Status epilepticus in Auckland, New Zealand: a year-long, prospective, hospital-based incidence study
Peter Bergin (Auckland, New Zealand)

**P12**
A rare case of simple focal non-motor status epilepticus
Magdalena Bosak (Warszawa, Poland)

**P13**
Drawback and strength of clinical research in status epilepticus
Maria Grazia Celani (Perugia, Italy)

**P14**
Nonconvulsive seizures and status epilepticus after liver transplantation in adults
Amy Crepeau (Phoenix, United States)

**P15**
A retrospective study on the demographic profile, clinical course, and management of children admitted with febrile seizures in a tertiary care hospital from 2010 to 2016
Jarren Mae Escape (Pasay, Philippines)

**P16**
50 consecutive cases of refractory status epilepticus in Ljubljana University Hospitals neurointensive care unit
Maša Hafner (Ljubljana, Slovenia)

**P17**
Epidemiology and treatment outcomes of status epilepticus in Lithuania
Agnė Kazlauskienė (Vilnius, Lithuania)
P18 – BEST POSTER
Incidence of status epilepticus in Salzburg in large population based study using the new ILAE definition
Markus Leitinger (Salzburg, Austria)

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New onset refractory status epilepticus with claustrum damage: electro-clinical features and outcomes
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**Basic Science**

**P01**

**Diurnal circulating microRNAs profiles in canines with naturally occurring epilepsy**

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**Background:** Epilepsy occurs in both humans and canines with similar clinical presentation, EEG, and response to pharmacotherapy, thus allowing canines to be a valuable model to understand this human condition. Diagnosis is difficult since clinical presentation can mimic other conditions and are often uninformative. There are currently no lab-based biomarkers for diagnosis or assessment of disease progression. MicroRNAs (miRNAs) are small noncoding RNA molecules that have a significant role in health and disease. Recently, circulating miRNAs have been identified in body fluids allowing them to be used as biomarkers. However, the diurnal variation in miRNA expression is not fully understood. We hypothesize that miRNA expression levels vary with the time of sample collection. Our long-term objective is to understand variation in blood miRNA expression following seizures.

**Methods:** Whole blood samples were collected twice (AM and PM) in PAXgene blood RNA tubes (Qiagen, CA) from five canines with naturally occurring epilepsy, maintained at the University of Minnesota Veterinary Medical Center. The canines experienced no seizures during the course of this study designed to understand the diurnal variation in miRNA expression. MiRNAs were extracted using PAXgene blood miRNA kit (Qiagen, CA) and analyzed by small RNA sequencing on an Illumina HiSeq 2000 platform. Statistical analyses were performed to determine the differences between groups.

**Results:** We identified ~180 unique canine miRNAs in whole blood. We observed limited differential expression of miRNAs between the two time points. Of the 16 miRNAs that showed more than 2-fold difference in expression, only 6 were statistically significant. Four out of the five dogs displayed upregulation of miRNAs in the AM compared to PM samples. This suggests that miRNA expression varies with the time of day.

**Conclusion:** Our data indicates that sampling time should be considered while interpreting miRNA expression analyses. We will perform further analysis to investigate the temporal regulation of miRNA expression following seizures in these dogs to identify optimal sample collection time points in a clinical setting. Novel biomarkers will provide diagnostic tools for clinicians, help patients and families, and enable clinical researchers to have a marker to track disease progression and response to treatments.

**P02**

**Developmental changes of adenosinergic system in hippocampal excitability after status epilepticus in immature and adult rats**

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**Purpose:** Status epilepticus (SE) induced in immature 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. The severity of functional alteration after SE was correlated with the levels of adenosine in hippocampus during brain development.

**Methods:** LiCl-pilocarpine SE was elicited in 12-day-old rats and hippocampal epileptic afterdischarges were studied in 15-, 18-, 25-, 32-, 60-day and 90-day-old rats with stimulation and recording electrodes stereotaxically implanted into dorsal hippocampus. Control animals...
received saline instead of pilocarpine. All age groups were formed by 10-14 animals. Animals recovered after surgery and threshold intensity for elicitation of hippocampal afterdischarges (ADs) was estimated. Biphasic 1-ms pulses were applied for 2 s at 60-Hz frequency. Stimulation series were applied six times with 20-min intervals. Thresholds and duration of ADs were evaluated. The dorsal hippocampus in 15- and 32-day-old rats (both control and experimental groups) was analyzed for concentration of adenosine by using HPL chromatography and microdialysis.

**Results:** Threshold for elicitation of hippocampal ADs was significantly higher in 15-day-old SE rats in comparison with control animals. The two older groups did not exhibit a difference between SE and control group but 32-day-old rats revealed significantly lower threshold intensity for SE rats than for control animals. Corresponding changes were found in AD duration after repeated stimulations – shorter ADs were recorded in P15 SE rats whereas duration of ADs was significantly longer in P32 SE rats in comparison with appropriate controls. These findings correspond to significantly increased level of adenosine in P15 SE rats and P32-day-old rats as the consequence of SE.

**Conclusion:** Our data demonstrated that during 20 days after SE induced at P12 complex changes of hippocampal excitability took place but did not persist in adults. P32 rats demonstrated higher excitability of dorsal hippocampus than their age-matched controls. These changes in hippocampal excitability might correspond to adenosine level after SE in this structure.

This study was supported by grants of the Grant Agency of the Charles University 2120192/2015 and a project of the Academy of Sciences of the Czech Republic No.67985823.

**P03**

**Differentially expressed long non-coding RNAs in the brain of pilocarpine-induced mouse epilepsy model**


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**Background:** Long non-coding RNA (LncRNA) is non-coding RNA longer than 200 base pairs in length. Recently, LncRNA has gained attention for its role in epigenetic regulation and diverse cellular activities. We attempted to evaluate the detailed profiles of dysregulated LncRNAs in the pilocarpine mouse model by isolating and separating the cortex and hippocampus, which are the most important structures in the epileptogenesis of TLE.

**Methods:** We performed extensive profiling of LncRNAs and mRNAs in the mouse pilocarpine model in specific brain regions, the hippocampus and cortex, and compared the results to those of the control mouse. Differentially expressed LncRNAs and mRNAs were identified with a microarray analysis (Arraystar Mouse LncRNA Expression Microarray V3.0). Then, gene ontology (GO) and pathway analysis were performed to investigate the potential roles of the differentially expressed mRNAs in the pilocarpine model. Protein-protein interactions transcribed by dysregulated mRNAs with/without co-dysregulated LncRNAs were analyzed using STRING v10 (http://string-db.org/).

**Results:** A total of 22 and 83 LncRNAs were up- and down-regulated (≥2.0-fold, all P< 0.05), respectively, in the hippocampus of the epilepsy model, while 46 and 659 LncRNAs were up- and down-regulated, respectively, in the cortex of the epilepsy model. GO and pathway analysis revealed that the dysregulated mRNAs were closely associated with a process already known to be involved in epileptogenesis: acute inflammation, calcium ion...
regulation, extracellular matrix remodeling, and neuronal
differentiation. Among the LncRNAs, we identified 10
LncRNAs commonly dysregulated with corresponding
mRNAs in the cortex. The STRING analysis showed that
the dysregulated mRNAs were interconnected around
two centers: the mTOR pathway-related genes and REST
pathway-related genes.

Conclusions: LncRNAs were dysregulated in the
pilocarpine mouse model according to the brain regions of
the hippocampus and cortex. The dysregulated LncRNAs
with co-dysregulated mRNAs might be possible therapeutic
targets for the epigenetic regulation of chronic epilepsy.

P04

Procalcitonin: dynamic changes and function
research in status epilepticus

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Background: Procalcitonin (PCT) is the precursor of
calcitonin and physiologically only produced by thyroid
gland, which increases under various inflammatory
circumstances. Recently, relationship between status
epilepticus and inflammatory arouse broad concerns.
Serum PCT levels measured at status epilepticus (SE) onset
are regarded independently associated with unfavorable
outcome. Also, excessive PCT is detected in CNS. Thus we
further confirmed the origin and the dynamic changes
of the serum PCT, then explored PCT’s effect in neuronal
excitability regulation.

Methods: Adult Sprague-Dawley rats were used in this
study. We use Lithium-pilocarpine injection (i.p) to induce
SE, Elisa to detected PCT, CRP and IL-6 in serum, Real-
timie PCR and Tricine–SDS-PAGE to measure mRNA and
protein levels of PCT in multiple tissues. We performed
immunohistochemistry to immunolabel the brain section
with PCT. Finally, whole-cell patch recording was used to
examine synaptic

plasticity changes after bath perfusion of PCT in
hippocampus.

Results: Serum PCT level significantly increased at 5 min
post SE, which was much earlier than serum CRP and IL-6
(30 min post SE). The increase of serum PCT also preceded
the increase of serum ALT, AST, CRE and BUN (1h). Both
RT-PCR and western showed ubiquitous and uniform
expression in multiple tissues throughout the body in
response to SE, especially in hippocampus.
A significant increase of PCT expression in the hippocampus
was observed at 30 min and reached the peak at 1h after
SE induction. Further immunohistochemistry showed the
activated astrocytes in the DG of hippocampus remarkably
upregulated the expression of PCT (SE 1h) upon challenge
by SE.
Whole-cell patch recording was performed to explore
the possible role of PCT in regulating the excitability of
neurons. In hippocampus slices, bath perfusion of PCT
(0.1Nm) increased both the amplitude and the frequency
of spontaneous excitatory postsynaptic currents (sEPSCs),
the number of action potentials (APs) and reduced the
paired-pulse ratio (PPR) of pyramidal neurons in CA1
region of hippocampus.

Conclusions: High level serum PCT from multiple tissues
associated with status epilepticus severity. It was also
upregulated in hippocampus during SE, and might increase
the excitability of pyramidal neurons and changes their
synaptic plasticity.

P05

Closed-loop gene therapy for intractable focal
epilepsy

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ABSTRACT NOT PUBLISHED
**P06**

**Action of adenosine A1 agonist on cortical epileptic afterdischarges is modified after status epilepticus in immature rats**

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**Background:** As a consequence of status epilepticus (SE) induced in 12-day-old rats reactivity of the brain to epileptogenic agents changes. This compromised reactivity might also be a reason for changed pharmacological sensitivity.

**Methods:** Lithium-pilocarpine SE was induced in 12-day-old rats and reactivity of cerebral cortex was tested at four intervals after SE – in rats 15, 18, 21 and 25 days old. Epileptic afterdischarges (ADs) induced by 15-s series of biphasic pulses with an 8-Hz frequency and stepwise increased current intensity (from 0.4 to 15.0 mA) repeated at 10-min intervals were used as a test. A specific agonist of A1 adenosine receptors CCPA was injected in a dose of 0.5 or 1.0 mg/kg intraperitoneally in the middle of stimulation series – after a 3.5-mA intensity. Duration of afterdischarges was measured and compared to that of control animals (pilocarpine was replaced by saline).

**Results:** A slow increase of duration of ADs was clearly interrupted by CCPA in 15- and 18-day-old rats but after two or three more stimulations it started to increase again. This increase was significantly steeper in control 12-day-old rats than in SE animals, this difference was no longer seen in older groups. The two older groups did not exhibit marked shortening of ADs after CCPA injection and difference between SE and control rats was negligible.

**Conclusion:** SE elicited in 12-day-old rats changes markedly but only transiently the anticonvulsant effect of adenosinergic system.

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**P07**

**Assessment of anti-seizure and neuroprotective effects of phenobarbital and memantine in a delayed-treatment rat model of organophosphate exposure**

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**Background:** Exposure to organophosphates (OP) or OP nerve agents can result in status epilepticus (SE), which can produce neuronal damage in the CNS. Early control of seizure activity could minimize mortality and neuronal damage. Current anti-seizure treatments for OP-induced SE are suboptimal; new treatments that more effectively control seizures are needed.

**Methods:** Male, Sprague Dawley rats (150-200 g) were implanted for recording the electroencephalogram (EEG) 1 week before treatment. On treatment day, SE was induced with diisopropyl fluorophosphate (DFP). One hour after SE onset, rats were co-administered midazolam and phenobarbital (Phe, 30 and 100 mg/kg), midazolam and memantine (Mem, 32 and 56 mg/kg), or midazolam and vehicle. EEG was recorded for 24 hr, rats were perfused, and brains were sectioned and labeled with Fluoro-Jade B. Neuropathology was assessed as the number of Fluoro-Jade B positive cells in 10 brain regions: dorsal CA1, dorsal CA3, hilus, ventral CA1, ventral CA3, amygdala, thalamus, and the parietal, entorhinal and piriform cortices.

**Results:** DFP induced a rapid and robust electrographic SE within minutes of administration. Co-administration of a high dose of phenobarbital (100 mg/kg) and midazolam 1 hr after onset of electrographic SE reduced the intensity of SE beyond the effect of midazolam alone. This effect was dose-dependent, as a lower dose of phenobarbital (30 mg/kg) had no effect. In contrast, co-administration of memantine (56 mg/kg) reduced the effect of midazolam, thereby exacerbating the intensity of DFP-induced SE. However, despite contrasting effects on seizure intensity, both compounds were neuroprotective, resulting in less neuronal death compared to midazolam alone.
Conclusions: These data demonstrate the feasibility and usefulness of this screening protocol in the detection of compounds that reduce seizure intensity and/or are neuroprotective, compared to midazolam alone. Despite having opposite effects on seizure intensity, both compounds significantly reduced neuronal death, suggesting that drug effects on neuronal death can be pharmacologically separated from effects on seizure intensity during SE. In regard to the development of compounds for the treatment of SE, this result demonstrates the importance of measuring the drug-induced neuropathological effects in addition to the drug effect on seizure intensity. Supported by the CounterACT Program, NIH Office of the Director and NINDS through an Interagency Agreement with the DoD.

P08 – BEST POSTER

Inhibition of monoacylglycerol lipase (MAGL) by CPD-4645 protects mice against refractory status epilepticus (SE) and its therapeutic effects are potentiated by the ketogenic diet

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Background: SE is a life-threatening condition and is commonly drug-refractory. Novel therapies are greatly needed to rapidly terminate seizures for preventing mortality and morbidity. MAGL is a key enzyme in the hydrolysis of the endocannabinoid 2-arachidonoylglycerol (2-AG) and its activity contributes to the brain source of arachidonic acid (AA) and eicosanoids. We investigated whether refractory SE, and the consequent cell loss and cognitive deficits, are reduced in mice by CPD-4645, a potent and selective irreversible MAGL inhibitor. We also investigated whether the effects of CPD-4645 were mediated by CB1 receptor activation by accumulating 2-AG or by reduction of AA availability to induce the eicosanoid cascade.

Methods: We induced diazepam-refractory SE in C57/BL6N male adult mice fed by normal diet or a ketogenic diet (KD; #F3666, Bio-serv) for 4 weeks, or in CB1 receptor knock-out (CB1R-KO) mice and their wild-type littermates. Following pharmacokinetic and pharmacodynamic characterization of CPD-4645, the compound or its vehicle was dosed 1 h and 7 h after SE onset (10 mg/kg, subcutaneously) in mice under continuous video-EEG monitoring. At the end of SE, mice were examined in the novel object recognition test, followed by brain analysis of neurodegeneration using Fluoro-Jade.

Results: CPD-4645 maximal plasma and brain concentrations (20 nM) were attained 0.5 to 2.0 h post-injection and were associated with cortical 2-AG increase and AA decrease (both around 4-fold). CPD-4645 injected in normal diet-fed mice progressively reduced spike frequency reaching 80% reduction 3h post-injection (p<0.01) followed by SE abrogation. SE duration was 4h shorter than in vehicle-injected mice (p<0.05). CPD-4645 also reduced Fluoro-Jade-positive neurons in CA1 pyramidal cells and amygdala (p<0.05) and rescued cognitive deficit. When injected in KD-fed mice, CPD-4645 virtually abolished SE in all mice with immediate effect. KD alone prevented CA1 neurodegeneration. CPD-4645 reduced SE severity and duration in CB1R-KO and wild-type mice similarly. The compound also reduced central inflammatory mediators such as IL-1β and COX-2.

Conclusions: CPD-4645 abrogated benzodiazepine-refractory SE and prevented neuronal cell loss; these effects were potentiated by KD. MAGL inhibitor also rescued cognitive deficits induced by SE. Modulation of eicosanoid pathway is a major mechanism underlying these therapeutic effects.
CLINICAL SCIENCE

P09 – BEST POSTER

Long-term epilepsy after post stroke status epilepticus (PSSE)

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Background: Stroke is one of the most frequent aetiologies of status epilepticus. However, in vascular aetiology it is unclear whether status epilepticus can be considered a risk factor for the development of remote seizures and if there is any specific factor predisposing to epilepsy. According to these data, we analysed the appearance of remote seizures after PSSE and the associated factors

Methods: We recruited 110 consecutive patients with PSSE from February 2011 to December 2016 and we selected those with no history of epilepsy. We collected different variables including demographics, baseline modified Rankin scale (mRS), data of the stroke index such as affected territory, stroke type, severity -NIHSS- and aetiology; and of status epilepticus itself such as: type of status, mSTESS, duration and treatment. We evaluated the development of epilepsy after PSSE at follow-up, and subsequently we compared those patients with those who remained seizure-free.

Results: We evaluated in total 64 patients without previous epilepsy. The mean age was 74.5±12.6 years old and 53.1% were male. The baseline mRS was 2 [1-3]. 57.8% of patients had an ischemic stroke and 48.4% had a middle cerebral artery territory infarction. The median NIHSS at index stroke was 8 [3-14] and it was 6.5 [2.25-12.75] at the onset of PSSE. The median time from the stroke to status epilepticus was 2.5 days [0-86]. 19 (29.7%) patients developed epilepsy at a median time of 182 days [70-484]. The estimated rate of epilepsy at first year in patients with NIHSS at the onset of PSSE>4 was 54.7% compared to 14.4% in patients with NIHSS≤4 (p=0.004). There was a tendency to develop epilepsy during the first year if temporal lobe was affected (58.8% vs. 15.7%, p=0.064). No relation was found regarding the other stroke variables, the time since the stroke to status epilepticus (p=0.317) nor the duration of the status epilepticus (p=0.845).

Conclusion: In PSSE, the stroke sequel (NIHSS >4) before the onset of status epilepticus and the presence of temporal lobe involvement were the only factors associated to the development of epilepsy at follow-up.

P10

Status epilepticus after cardiac arrest - electrographic characterisation of the ictal-interictal continuum

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Background: Nonconvulsive status epilepticus is a common cause of persistent coma after cardiac arrest. These patients often show rhythmic or periodic EEG patterns along an ictal–interictal continuum. Unified terminology is lacking. American Clinical Neurophysiology Society has published a standardised terminology for critical care EEG. We applied the terminology on simplified continuous EEG and described the characteristics of electrographic status epilepticus (ESE) in comatose patients after cardiac arrest.

Methods: Retrospective cohort study of consecutive patients treated with targeted temperature management and monitored with simplified continuous EEG. Patients
with ESE were identified and electrographically characterised until 72 hours after ESE start using the standardised terminology. Patients fulfilling the strict criteria of unequivocal ESE were compared to patients with rhythmic or periodic borderline patterns (≥ 1Hz discharge frequency) defined as possible ESE.

Results: ESE occurred in 41 of 127 patients and 22 fulfilled the criteria for unequivocal ESE, which typically appeared transiently and early. Three of the four survivors had unequivocal ESE, starting late from a continuous background. 19 patients fulfilled our criteria for possible ESE. There were no differences between the groups of unequivocal ESE and possible ESE regarding outcome, neuron-specific enolase levels or prevalence of clinical convulsions.

Conclusion: ESE is common after cardiac arrest. The distinction between unequivocal and possible ESE patterns was not reflected by differences in clinical features or survival. Sporadic patients with ESE have a favourable outcome, regardless of using strict or liberal ESE definitions. Unequivocal ESE after cardiac arrest may easily be missed without early and continuous EEG-monitoring.

P11 – BEST POSTER

Status epilepticus in Auckland, New Zealand: a year-long, prospective, hospital-based incidence study

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Background: To determine the incidence, causes and outcomes of Status Epilepticus (SE) in Auckland, New Zealand, using the EpiNet database.

Methods: All patients more than 4 weeks of age who presented to the 5 public hospitals within Auckland city (population 1.6 million) with SE (defined as seizure duration exceeding 10 minutes) between 6th April 2015 and 5th April 2016 were identified using multiple overlapping sources of information. Post anoxic SE was excluded. Emergency department (ED) presentations and hospital discharges were reviewed daily, and referrals received from physicians, neurophysiology, and intensive care units. Baseline health economics, clinical details, treatments, and outcomes for each episode of SE were entered into the EpiNet Database. Patients are being followed up at 1 and 2 year intervals.

Results: Hospital records for > 6000 presentations with possible seizures were reviewed. 624 episodes of possible SE were identified by study nurses. To date, 597 of these presentations (95%) have been reviewed by a neurologist. 442 presentations in 386 patients were considered definite or probable SE; 56 patients had > 1 episode of SE during the year; 3 patients had 5 episodes, and 1 had 9 episodes of SE. The incidence of primary and recurrent SE in Auckland is 27 episodes (24 persons) per 100 000 per year. 60% of episodes lasted > 30 minutes. 56% of episodes ceased before arrival at ED. 50% of patients received benzodiazepines before presentation to hospital. 48% received iv AEDs in ED, with a median time to treatment of 27 minutes. 51% of the patients were aged <15, 35% were 15-59, and 14% over 60 years. A cause for the SE was identified in 76%. 44% of episodes in children were associated with fever. 81% were back to normal by discharge. 52% of patients had known epilepsy before the SE. 23 patients (7%) died within the study period.

Conclusion: This study has determined the incidence, aetiology, treatment and outcomes of SE in New Zealand. A form to collect comprehensive data on SE in the EpiNet database has been developed, and can be used for multicentre cohort studies and randomised controlled trials.
A rare case of simple focal non-motor status epilepticus

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40 old female with a history of complex partial seizures since the age of 20 presented to the neurology service because of increased seizure frequency and continuous fear for 3 days (patient reported this fear as an unpleasant anxiousness before upcoming seizure). Her habitual seizures were always preceded by fear, followed by arrest of activity, staring, and oral automatisms. She had 1-2 complex partial seizures per month and rare tonic-clonic seizures. She was treated with levetiracetam (1250 mg/day) and topiramate (200 mg/day). Brain MRI revealed no pathology. In previous EEG, theta waves and sharp waves were recorded in the left temporal region. Last EEG obtained in 2012 showed no abnormality (fig. 1).

The neurological examination was unremarkable. The patient was conscious, fully oriented to person, place, and time. Limb or oral automatism was not observed. Involuntary movements were not observed. EEG was performed and showed continuous, rhythmic sharp activity in the left frontotemporal region (Fig. 2).

Affective focal status epilepticus was diagnosed. After 10 mg of intravenous diazepam, no changes in neither patient symptoms nor EEG were observed. After administration of 3000 mg intravenous levetiracetam, the fear was reportedly resolved. Control EEG showed no abnormality (fig. 3).

Simple focal status epilepticus with fear as the only clinical expression may represent a diagnostic challenge. When fear is the only prominent behavioral feature, seizures may be diagnosed as panic attacks, thus leading to erroneous therapy. In such situations, electroencephalography is an essential tool in differentiating between psychiatric disorders and epileptic events.

Drawback and strength of clinical research in status epilepticus

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**Background:** Nowadays there is a wide variability in treatment of Status Epilepticus (SE) in neonates, children and adults.

**Method:** We performed a systematic review of all truly Randomized Control Trials (RCTs) published in any language, over a period of 7 years (1.01.2009–31.12.2015), on interventions in Epilepsy in order to analyze the quality and methodological aspects of research in this field. We searched the Cochrane Central Register of Controlled Trials and MEDLINE. For each pertinent trial a neurologist filled out a computerized form saved in a data base, from which RCTs on SE were selected.

**Results:** We report the preliminary analysis conducted to 31.12.2013, the subsequent time span is ongoing. We examined 949 published papers on Epilepsy; only 167 were truly RCTs and 16 of them were focused on SE or acute seizures. All but one were in English, one was in Chinese, 7 had a precise definition of SE in the inclusion criteria, while 9 studies considered “acute prolonged seizures”, in 6/16 was it stated that seizures were 5 or more minutes long. 75% were single centre-based. People under 2 or >80 years of age were less investigated. Randomization appeared adequate in 68.7%, but sample size calculation was appropriate only in 56%, source of funding was not reported in 43% while 12.5% of trials were clearly for profit. We detected a wide difference between outcome measures going from “time to next seizure” to “clinical seizure remission within 10min” or “seizure free within 24h”.

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**Conclusion:** Universally accepted definitions of premonitory, early, established and refractory SE should be better applied. The most recent definition of SE proposed by the ILAE Task Force with two operational dimensions (t1 and t2) could help to overcome this issue. Weaknesses in design, analysis and an over wide selection of outcome measures highlight that research should have a better methodological quality and reporting. A low percentage of declared conflicts of interest in the included RCTs are also identified. The body of evidence is small and weak. It is important to help researchers perform meta-analysis and produce good clinical evidence to standardize practice.

**P14**

**Nonconvulsive seizures and status epilepticus after liver transplantation in adults**

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**Background:** Adults undergoing liver transplantation are at risk for neurologic complications from a myriad of sources, including cerebrovascular events, opportunistic infections, posterior reversible encephalopathy syndrome and other immunosuppressant-related neurotoxicities. These neurologic complications all carry a risk of seizures and status epilepticus, which can be difficult to identify in these patients, as they are commonly encephalopathic due to underlying liver disease. We aimed to identify the incidence of nonconvulsive status epilepticus and seizures in the period after liver transplantation.

**Methods:** This was a single center, retrospective study. All patients undergoing liver transplantation between 2011-2016 were identified using the database maintained by the liver transplant service. This database was cross-referenced with the EEG database, searching for inpatient EEGs performed on these patients in the 3 month period post-transplant. EEG findings and relevant clinical data were obtained by reviewing respective medical records.

**Results:** Between January 2011 and December 2016, a total of 450 liver transplants were performed on 439 individual patients. Thirty-one of these patients had inpatient EEGs performed within the 3 month post-operative period. Three of these patients had continuous EEG monitoring. Prior to the EEG, 4 patients had a witnessed clinical seizure, and 2 patients had possible seizures. In the majority of cases (n=22), the indication was altered mental status. None of the EEGs were normal: 2 demonstrated mild (theta) slowing, and the remainder showed moderate (delta) slowing. Triphasic waves were present in 10 of the recordings. Interictal epileptiform discharges were present in 3 recordings, periodic discharges present in 2, and only 1 patient had electrographic seizures and nonconvulsive status epilepticus.

**Conclusions:** Despite high risk for neurologic complications in this patient population, we found only 1 patient with nonconvulsive seizures and status epilepticus. Witnessed clinical seizures did occasionally precede the EEG, but the most common indication was altered mental status. These data suggest that while encephalopathy was common as evidenced by the lack of any normal EEGs, subclinical seizures may be relatively uncommon in this population. Relatively low utility of inpatient standard and continuous EEG may have missed cases.

**P15**

**A retrospective study on the demographic profile, clinical course, and management of children admitted with febrile seizures in a tertiary care hospital from 2010 to 2016**

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**Background:** Febrile seizures (FS) occur in 4-5% of children and account for the majority of seizures seen in children in emergency rooms. Local clinical practice guidelines for FS were developed in 2004. We undertook this study to look at the demographic profile of children admitted with FS, review their clinical course, diagnostic evaluations, drug management, etiology of fever, and neurological outcome. It is our hope that the information gained from this study would aid in the revision and adaptation of local clinical
Objective: To describe the clinical profile, fever etiology, clinical course, diagnostics and neurological outcome of patients admitted with febrile seizures. Data gathered was compared with clinical practice guidelines.

Methodology: Retrospective descriptive study that reviewed hospital records of children admitted with febrile seizures over 7 years.

Results: A total of 373 patients comprised the sample population. Eighty-nine percent were simple febrile seizures. Ages ranged from 3 to 91 months with the largest group in the 13-18 month old range. There was male preponderance and higher number of admissions during the rainy season. Family history was common, paternal side dominant. The most common cause of fever was upper respiratory tract infection and systemic viral Illness. CBC was done in all patients. EEG’s were done in 27.35% of patients; 41% done in simple febrile seizures. Intravenous fluids and antipyretics were given and diazepam was ordered in all patients; antibiotics were given to 62.2% of patients. Patients with complex febrile seizure are more likely to be referred to subspecialist and/or have more laboratory and imaging tests. Neurological outcome was normal.

Conclusion: This study showed male preponderance, increased paternal family history and seasonal variation in FS. In spite of upper respiratory tract infection and systemic viral diseases being the most common cause of fever, majority of patients received antibiotics. There was noted deviation from approved clinical practice guidelines.

P16

50 consecutive cases of refractory status epileptics in Ljubljana University Hospitals neurointensive care unit

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Background: Refractory status epilepticus (rSE) is a life threatening neurological emergency with significant mortality and morbidity. It is defined as status epilepticus (SE) that continues despite treatment with adequate dosage of benzodiazepine (first line) and one intravenous antiepileptic drug (AED). Treatment of rSE requires admission of the patient to intensive care unit and in most cases treatment with general anaesthesia. Super-refractory status epilepticus (srSE) is rSE that continues or recurs 24h after the onset of adequate anaesthetic therapy. Objective of our study was to evaluate data on clinical course, therapeutic interventions and outcome of all rSE patients admitted to our neurointensive care unit (NICU) in 2014-2015.

Methods: We retrospectively reviewed medical records of patients admitted to the NICU for treatment of rSE in years 2014 and 2015. We looked at aetiology and type of SE, management before admission to NICU (first and second – line treatment of SE), sedative and AEDs used in NICU, duration of sedation and ventilatory support, time to SE termination, length of stay in NICU, use of EEG monitoring and treatment outcome.

Results: 50 cases of rSE were identified, 24 were women, 26 men, average age was 56,1 years. 32 (64%) were tonic-clonic SE, 11 (22%) focal motor, 3 (6%) nonconvulsive and 4 (8%) with prominent motor symptoms evolving into nonconvulsive SE. Aetiology: 22 (44%) SE were acute symptomatic, 16 (32%) remote symptomatic, 4 (8%) progressive symptomatic and the remaining 8 (16%) had no identifiable cause. 26 patients
(52%) have had known epilepsy prior to SE. 6 patients (12%) had srSE. In total 4 patients (8%) died, 2 of those had srSE. 14 patients (28%) had standard 20 min EEG (single or repeated), long term EEG monitoring was performed in 12 patients (24%). The remaining 48% of patients had no EEG prior to discharge from NICU. EEG findings, AED use, and outcome will be presented and discussed.

Conclusions: We found suboptimal adherence to SE first and second line treatment protocols and underuse of EEG and in NICU. Data provided by this study will serve as a basis for improvement of treatment protocols and prospective research on rSE treatment.

P17

Epidemiology and treatment outcomes of status epilepticus in Lithuania

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Background: Convulsive status epilepticus (CSE) is one of the most common neurological emergencies. This research concerns epidemiology, etiology and outcomes of CSE in Lithuania.

Methods: Retrospectively were analyzed cases of patients, who experienced CSE during ten years period and were admitted to Vilnius hospitals. Statistical methods we used – Student t-test, Mann-Whitney U, χ² test, correlation tests.

Results: 1472 CSE cases were included: 1002 cases of adults (53.8±16.1 years) and 468 cases of children (meanly 6 years old (0.08-17)). A crude incidence – 18.32/100,000/year among grown-ups and 31.8/100.000/year among kids in Vilnius, Lithuania. 68.2% (p<0.001) adults (70.1% men, p<0.001) and 42.8% children had previous history of epilepsy. The most frequent cause of CSE in adult patients with epilepsy was alcohol intoxication (36,1%). It caused CSE for men 5 times more often than for women (p<0.001). Onset of epilepsy and inappropriate treatment in children entailed most of the cases (32,7%). The mean duration of CSE – 5.41 h (5min-528h, median 2.5). Males experienced shorter CSE (meanly 5 hours) than females (meanly 6 hours) (p=0.09). The later was treatment initiation, the longer was CSE (p<0.001). CSE was shorter in younger patients (meanly 10.9 years old), while patients meanly at age of 48.2 years experienced longer CSE (p<0.001). For adults CSE caused by structural CNS lesions was longer (p=0.002) while metabolic etiology determined shorter duration (p<0.05). The mean duration of hospitalization was 6 days (1-57 days). Children spent less days in hospital (5.2 vs. 6.4 for adults) (p<0.001). The length of hospital stay and duration of intensive care unit (ICU) stay was longer for older (p<0.001) patients, and for those with longer CSE duration (p=0.003, p<0.001). Mortality was 1.2/100.000/year for adults, while case fatality – 6.18%. We found a higher fatality rate among older (p<0.001), those adults without epilepsy (p=0,002), longer CSE (p<0.001) and those who were admitted to ICU (p=0,016).

Conclusions: an incidence of CSE 18.32/100,000/year (adults) and 31.8/100.000/year (children), mortality – 1.2/100.000/year. Negative prognosis comes for older and with longer CSE. Studies concerning CSE in Baltic region are scarce so we suggest this research could invite further thought improving accessibility and effectiveness of help.

P18 – BEST POSTER

Incidence of status epilepticus in Salzburg in large population based study using the new ILAE definition

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Objective: the International League Against Epilepsy
proposed a new classification of Status Epilepticus in 2015. According to the new classification, the inclusion criteria for different forms of Status epilepticus have changed. To our best knowledge, no population based study exists on the incidence of status epilepticus using the new classification. We present a retrospective study on the incidence of status epilepticus in the city of Salzburg, Austria.

Methods: for this study we retrospectively collected data from all the patients admitted in the Christian Doppler Klinik, University Hospital, Salzburg between 2011 and 2015, who received the diagnosis “status epilepticus” at any point during the hospital stay (admission diagnosis, working diagnosis, final diagnosis, EEG diagnosis etc.). The patients were then filtered for home address in Salzburg City (150 936 inhabitants). The episodes of status epilepticus were defined with the new definition of Status epilepticus. Then the incidence was calculated by using population data of Salzburg City as reported by the Statistik Austria. We analyzed In house mortality and 30 day mortality, antiepileptic drug and refractoriness of status epilepticus.

Results: we identified 514 patients who suffered from status epilepticus in the investigated 5 years. This results in an incidence of 113/100,000 per year. The majority of patients had status with major motor phenomena; 52.3% of all patients had convulsive status epilepticus.

Conclusion: In this population based study on the incidence of status following the new definition, we found higher incidence rates compared to the previous population based studies using the conventional diagnostic criteria.

P19

New onset refractory status epilepticus with claustrum damage: electro-clinical features and outcomes

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Background: new-onset refractory status epilepticus (NORSE) is a rare but challenging condition occurring in a previously healthy patient and with no identifiable cause. We characterize the electro-clinical features and outcomes in a group of patients with a typical MRI sign characterized by bilateral lesions of the claustrum.

Methods: demographic, clinical, EEG, imaging, laboratory data are described in previously healthy adults (> 16 years of age) with new-onset status epilepticus (SE) showing brain MRI evidence of bilateral hyper-intense alteration of the claustrum.

Results: 12 personal and 19 previously published cases were included, for a total of 31 patients (17 females; mean age of 25 years). Twenty-eight patients presented fever before SE by a mean of six days. SE was considered refractory/super-refractory in 74% of the patients, requiring third lines agents and intensive care unit admission (for a median of 15 days). Focal motor and tonic-clonic seizures were observed in 90%, complex partial seizures in 14%, and myoclonic seizures in 14% of the cases. Bilateral hyper-intense claustrum was always observed after SE onset (mean of 10 days). Other limbic (hippocampus, insular) alterations were present in 53% of the patients. Within the personal cases, extensive search for known auto-antibodies was inconclusive, however in seven out of 11 patients CSF lymphocytic pleiocytosis was observed, while oligo-clonal bands were present in three cases. One subject died during the acute phase, one in the chronic phase (probable SUDEP); one patient developed a persistent vegetative state. Among survivors, 80% developed drug-resistant epilepsy.

Conclusions: febrile-illness related SE with claustrum hyper-intensity represents a homogeneous condition with defined electro-clinical features and with a probable autoimmune aetiology. A better characterization of de novo SE is mandatory for the search of specific etiologies.
Myoclonic status epilepticus in late onset myoclonic epilepsy in down syndrome with post traumatic epilepsy

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Background: Late Onset My Epilepsy (LOMEDS) is characterised by late onset progressive myoclonic epilepsy associated with dementia that begins during or after fifth decade in persons with Down syndrome (DS) (Genton, Paglia, 1994). Clinical Features are massive myoclonia, generalised tonic clonic and reflex seizures.

Methods: Susan (S.), a 56 ys woman, affected by DS, underwent to our attention cause continuous myoclonic jerks, involving arms and trunk in person threated with VPA 500, PB 100 and Clonazepam 6 drops/ die. Affected also by Hypotiroidism.

On February 2011 had subdural hematoma due head injury after a fall of unknown cause. Brain RMN, done 1 year later, showed multiple post traumatic cerebromalacic areas (bilateral frontal, right parietal and left occipital). She began to have rare generalized tonic clonic and cognitive seizures, threated with PB 100 and LEV 1000.

On 2013 was observed occasional myoclonic jerks, threated, initially, was added VPA 500 mg stopped for adverse events (mood depression, tremors); then assumed PB until 150 mg and LEV 1500 mg/die. Diagnosis of LOMEDS was put over 2 years ago.

On the day of our observation myoclonic jerks were permanently present after awake, early in the morning, with mild impairment of consciousness. Video EEG registration showed continuous discharges of polyspikes and wave, focal or generalized: on right fronto-temporal or bilateral synchronous brief sequences, with concomitant myoclonic limbs jerks (see video). Unfortunately EEG was made without EMG deltoid muscles electrodes.

Results: We didn’t decide to threat strongly myoclonic status epilepticus using i.v. benzodiazepines or VPA or LEV to avoid a worsening of conscience status and gived only an oral further dose of clonazepam; myoclonic status gradually disappeared only when she was back home.

Conclusions: We report this case in order to complexity of etiology for considering the most appropriate strategy to threat a non common form of status epilepticus, the myoclonic one, also in order of the risk of evolution in a convulsive status. The case suggests some questions. 1) Was it a myoclonic status or a motor focal or a “cocktail” of both? 2) Was it corrected avoid use of benzodiacepine and more? 3) May we consider the status events, in the context of dementia progression, due to concomitant multiple brain lesions and LOMEDS, a reason to increase antiepileptic therapy?
accounted in 67.3% of the patients with previous seizures and in 32.7% of patients with no history of epilepsy. The other causes in our series were alcohol-withdrawal, cerebrovascular disease, cerebral tumors or trauma, infection, metabolic disorders, anoxia. SE was never the initial manifestation of further epilepsy. 144 patients (92.3%) developed generalized tonic-clonic SE and only 3 (1.92%) patients presented with nonconvulsive SE. In our study SE was terminated by intravenous diazepam followed by intravenous phenytoin in 75% of cases, but in the patients with continuous SE we used second line drugs as phenobarbital (32.4%). A poor GOS outcome of SE was correlated with cerebral infarction and increased age, low mortality rates were noted in alcohol and nAED etiologies.

Conclusions: Cerebrovascular disease and nAED were the most prominent causes of SE in this study. GOS scores and etiology SE showed a better outcome in patients with cancelation / AED noncompliance and unfavorable outcomes in elderly patients and those with acute brain injury such as stroke or cerebral anoxia. Low incidence of non-convulsive SE requires a better clinical evaluation and continuous EEG monitoring. More than half of patients were young adults and nAED was the main cause of SE, which may be prevented by patient and family education.

P22

Super-refractory status epilepticus or degenerative encephalopathy with rapid progression? A case report


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Background: Nonconvulsive status epilepticus (NCSE) may be distinguished with difficulties from acute/subacute onset encephalopathies (metabolic, toxic, post-anoxic, spongiform), particularly in de novo cases.

Methods and Results: We report the case of a 57-year-old man, otherwise normal, with positive family history for epilepsy, who was referred to us for a suspected NCSE. Few weeks after a febrile illness, he started to experience brief episodes of right head and trunk deviation with loss of consciousness, associated with progressive behavioral changes (irritability, aggressiveness), confusion and speech disturbances. After a month an MRI showed cortical hypersignal in the left fronto-temporo-parietal regions in DWI images. An EEG showed sequences of sharp-wave/spike-wave-and slow-wave complexes on the left fronto-temporal regions. The CSF analysis showed a mild proteinoracchia and Tau protein increase; oligoclonal bands, viral PCR, tumor and autoimmune markers, lactate/pyruvate, 14.3.3 protein were negative; the search for prion protein was negative on CSF and nasal brush. Total body CT scan and FDG PET were unremarkable. Despite the treatment with numerous antiepileptic (AE) drugs, anesthetics, IVIg and steroids, and ketogenic diet, he showed a progressive clinical worsening. Three months after onset, having interrupted all anesthetic drugs, the patient was still in coma with spontaneous and induced myoclonic jerks of upper limbs and of oro-facial region. The EEG showed bilateral periodic EEG pattern with runs of fast epileptic discharges associated with increments in myoclonic activity. Repeat MRI showed DWI and FLAIR hypersignal in the basal ganglia bilaterally, and a progressive severe cortical and subcortical atrophy.

Conclusions: The new onset of super-refractory status epilepticus, after a mild febrile illness, in an otherwise normal man, suggests a new-onset refractory status epilepticus (NORSE). However, the severe AE drug-resistance, the rapidly progressive clinical and radiological abnormalities and the EEG periodic pattern, do not exclude the possibility of a rapidly progressive degenerative encephalopathy.
Audit of neurological considerations, treatment protocol and outcome of Status Epileptics from LAMICs (Low and Middle income countries)

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Background: Status epilepticus (SE) is the most serious expression of epilepsy. Factors associated with mortality have been adequately identified in population based studies from high income countries but similar studies from low and middle income countries (LAMIC) are few and far apart. We aim to report a systematic review of factors associated with mortality in SE in LAMICS.

Methods: The literature search of studies from internet using terms “status epilepticus” and ‘incidence’, ‘etiology’, ‘treatment’ and ‘mortality’. All abstracts and full articles of identified relevant abstracts were reviewed in which data on incidence, etiology, seizure type and factors associated with mortality were available. From the initially identified 1023 articles, all but 177 were excluded. The primary outcome variable was in-hospital mortality during that episode of admission regardless of the duration of hospitalization. The effect of explanatory variables such as age, etiology, treatment protocol, delay in initiation of treatment, geographical location of the study, economic status and calendar period were also recorded.

Results: Twenty six studies spanning 25 years (1989-2014) representing thirteen countries of Asia, Africa, South America and Europe were analysed. The cohort had 3734 patients, 2391 adult and 1572 males with 2794 patients from the upper middle income and 940 patients from the lower and lower-middle income countries. The aggregated result of nine trials showed that risk of death is 1.3 times less in patients younger patients as compared to older age group (OR=1.33; p=0.006). The pooled analysis of five studies showed that mortality risk increases by 2.8 times with delay in treatment beyond 1 hour (OR=2.8; I²=0%). Among all etiologies, 23% patients had SE due to acute central nervous system infections and pooled analysis of seventeen studies showed that it increases mortality risk by 2.8 times (OR=2.83; I²=7.2). There is geographical variation in the mortality rates in SE with 1.2 times higher mortality in the Asian countries as compared to the rest of the world (OR=1.2;p=0.0025).

Conclusions: Delay in initiation of treatment and infections are modifiable factors contributing to high mortality in SE in LAMIC and their awareness can lead to development of strategies to reduce associated mortality.

Risk of prolongation of adult epileptic seizure

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Background: Current guidelines define status epilepticus as epileptic seizure continuing for >5 minutes or manifesting as recurrent seizures without return on consciousness in between. Factors predicting seizure prolongation have been studied mostly in pediatric material. The present study describes the clinical characteristics of convulsive seizures the duration of which exceeds 5 minutes, and the risk of the situation to develop into refractory status epilepticus.

Methods: Retrospective study of all cases of convulsion, both continuous and recurrent, (N=1205, ICD codes G40 and R56) admitted to the ER of a tertiary hospital (population base 1,4 million) over 12 months.

Results: The convulsion lasted over 5 min in 13,0 % of all cases of hospital-treated acute convulsion. The seizure was the first epileptic manifestation in 9,2 %, while 82,6 % had experienced seizures previously and 71,2 % had been previously diagnosed with epilepsy. Notable differences in predisposing factors between prolonged seizures (5-29 min), established status epilepticus (30-59 min), refractory status epilepticus (over 60 min) and recurrent convulsions were found. The most common predisposing factors in the four groups included alcohol (18 %, 22 %, 13 %, 26
previous ischaemic stroke (14%, 25%, 17%, 11%), previous brain operation (14%, 17%, 26%, 7%), brain trauma (16%, 22%, 4%, 15%) and brain tumor (11%, 6%, 22%, 22%). 18% of all seizures lasting over 5 min ceased spontaneously. First-line treatment was successful in 44%, 31%, 26% or 26%, the second-line treatment in 26%, 17%, 17% or 33%, and third-line treatment in 12%, 53%, 61% or 41% of each group. The risk for prolongation over 30 min was 55%. Subgroup analysis of continuous convulsions (5-9, 10-14, 15-19, 20-24 or 25-29 min.) showed that the risk increased in relation to duration of convulsion, there being a marked rise at 10-15 min.

Conclusion: Prolonging convulsions should be treated aggressively within the first ten minutes to minimize the risk of refractory status epilepticus.

P25

Socioeconomic outcome and quality of life in adults after status epilepticus at three German university hospitals

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Background: There is a lack of data concerning socioeconomic outcome and quality of life in patients after status epilepticus (SE) in Germany.

Patients and Methods: Adult patients treated due to status epilepticus (SE) at the university hospitals in Frankfurt, Greifswald, and Marburg were asked to fill out a questionnaire regarding long-term outcome of at least three months after discharge.

Results: A total of 80 patients (mean age: 58.9±18.0 years, range: 21-97; 57.5% female) participated. An acute symptomatic etiology was present in 26.3%, a new onset SE in 21.3%, a remote symptomatic SE in 42.5% and other or unknown etiologies in 10%. 58.9% of the cases had a non-refractory SE, 27.5% a refractory SE and 13.8% a super-refractory SE. Before admission a modified Rankin Scale (mRS) of 0-3 was found in 82.3% (65/79) and one of 4-5 in 17.7% (14/79). On discharge 31/79 patients (39.2%, p=0.004) had an unfavourable mRS of 4-5. The majority returned home (50.6% [40/79]), 32.9% (26) entered a rehabilitation facility, while 12.7% (10) were transferred into a nursing home and 3.8% (3) in another hospital. At the time of follow-up of at least three months, 21 patients (26.6%) lived at home without any help, 33 (41.8%) depended on aid of their families or partners and 9 (11.4%) of ambulatory nursing care; 15 patients (20.3%) lived in a nursing home. The mRS at follow-up did not differ from the one at discharge; 61.6% (45/73) presented a mRS of 0-3 and 38.4% (28/73) a mRS of 4-5. A care level (Pflegestufe) was attributed to 56.9% and a grade of disability to 79.7%. Only 9 of 48 patients of working age (18.8%) had been employed at follow-up. The number of AEDs did not differ at follow-up as compared to discharge. 26/71 patients (36.6%) took ≥3 AEDs (vs. 26/79; 32.9%), 14/71 (19.7%) 2 AEDs (vs. 26/79), 28/71 (39.4%) 1 AED (vs. 26/79) and 3 patients (4.2%) did not take any anticonvulsive medication.

Discussion: Patients after SE show substantial impairments in their daily activities and independence. Results of this survey are probably biased due to SE associated mortality and morbidity.

P26

Status epilepticus at a Tertiary Hospital

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Background: The department of Neurology at Rigshospitalet, Copenhagen, being the largest in Denmark, covers, with regard to epilepsy care, the central and south Copenhagen, from two locations. The unit covering the central Copenhagen is a tertiary center for patients with status epilepticus (SE) in close cooperation with the departments of Neurophysiology (DoNP) and
Neuroanaesthesiology. It is as well the only service offering cEEG and emergency EEG all days of the week in the Capital Region of Denmark (pop. 1.7 mio.). The aim of this retrospective review was to estimate the frequency of status epilepticus in the catchment area during the period 2014-2016, as part of an effort to increase the efficiency of diagnosis and management of SE at our site.

**Methods:** We used the database of the DoNP to identify patients referred to EEG/cEEG on suspicion of SE and chart relevant statistics. Data were analysed with Stata IC 14.2.

**Results:** During 2014-2016 1151 patients, average age 58 years (range 0-97), 45 % female, were referred to EEG on suspicion of SE. cEEG monitoring was not included in the present analysis. A total of 1545 EEGs was performed on this indication. The suspicion of SE was confirmed in 141 patients (12 %). The frequency of confirmed SE cases was rather stable across the period, 2014: 48, 2015: 57, 2016: 36.

**Conclusions:** This is a preliminary report and does not allow any firm conclusions. However, it appears that the proportion of confirmed SE cases was low. More critical clinical judgment would probably allow an increased capacity for other diagnostic purposes or epilepsy surgery monitoring.

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**P27**

**A non-typical epileptic reaction in a patient with insulinoma of the pancreas: a case report**

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Extreme hypoglycemia in cases with insulinoma may be clinically manifested with epileptic reactions, most frequently described in literature as generalized tonic-clonic seizures.

We present a case of a 30-year old man who was hospitalized at the Clinic of Neurology of the University hospital “St. George” in Plovdiv, Bulgaria, because of frequent seizures (2-3/ week), manifested with impaired awareness, aggressiveness, agitation, and confusion, mainly in the morning. The patient had been initially treated in a psychiatric clinic, afterwards he was diagnosed with epilepsy and was treated with valproate without success. During his stay in the Clinic of Neurology the medical staff observed a couple of focal seizures with impaired awareness, turning head aside, fixed eyes, followed by aggressiveness, agitation, and postictal confusion. Extremely low levels of blood sugar were measured in the morning – up to 1.3 mmol/l (referent limits 4.1-5.9 mmol/l). The polysomnography recording showed episodes of high voltage synchronous slow activity in all derivations at the time of the described above seizures and hypoglycemia, which were coped with 40% glucose solution. Insulinoma in contact with the tail of the pancreas was verified as a metabolically active lesion on PET/CT. The patient was directed to a surgical department for biopsy and treatment. Seizures became less frequent when the patient was restricted to a regular carbohydrate diet.

We consider the reported case is a diagnostic challenge because of the type of clinical manifestations and the absolute necessity of highly specialized neuroimaging investigations for etiology precision.

**P28**

**Hippocampal sclerosis in evolution - 3 adult cases**

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**Introduction:** Transient MRI findings have been described in patients who experience prolonged seizures, restricted diffusion and T2 signal weighted abnormalities are thought to represent areas of vasogenic or cytotoxic oedema which when followed longitudinally may resolve or persist. In some cases if the seizure-induced neuronal injury is severe enough areas of atrophy and gliosis may develop.
Clinical Cases: Here we present three cases of de novo status epilepticus in patients with no prior history of epilepsy. We describe their periictal findings and follow up scans. A 55yr old man presented after prolonged complex partial SE accompanied by secondary generalisation. On arrival to hospital he required intubation and transfer to ICU. Imaging within 72hrs of seizure onset revealed increased signal in the T2 and FLAIRE sequences of both mesial temporal lobes with changes more pronounced on the right which were accompanied by restricted diffusion in that area. Follow up studies at 2 and 6 months showed resolution of the restricted diffusion but the development of right sided hippocampal sclerosis. The second patient a 78 year old lady had prolonged upper limb automatisms followed by two generalised tonic-clonic seizures without clear recovering in between. She required ventilatory support and transfer to ICU. Her MRI revealed high-signal in the right hippocampus and mesial temporal structures again with restricted diffusion. These changes persisted at one week despite electrographic and clinical cessation of her seizures. The third patient a 47 year old man with multiple co-morbidities had a prolonged convulsion at home and refractory status epilepticus. His MRI showed bilateral T2 and FLAIR hyperintensities in both mesial temporal lobes with correlated restricted diffusion. These changes though less severe persisted at 3 weeks post the event. Further longitudinal imaging studies are planned for both the second and third patients.

Conclusions: Here we describe three adult cases who had no pre-existing diagnosis of epilepsy who during their periictal period had diffusion, FLAIR and T2 MRI changes. Some of the changes persisted and in one case where longitudinal 6month follow up is available adult onset hippocampal sclerosis has developed. We argue that the presence of periictal MRI changes can be used as surrogate marker of seizure severity and possibility of development of mesial temporal sclerosis in the future.

OUTCOME STUDIES

Super-refractory status epilepticus: survivors and non-survivors

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Background: Super refractory status-epilepticus (SRSE) is defined as status-epilepticus that continues or relapses despite 24 hours of general anaesthesia. SRSE is mainly seen in patients with severe acute brain insult or in the entity known as NORSE.

Method: Multicentre retrospective review based on daily recorded EEG of patients with SRSE at King’s College hospital, London, UK; East Kent Hospitals, UK; and University Hospital Marques de Valdecilla, Spain, from 2013 to 2016.

Results: Ten cases were found. Six presented with viral symptoms, one with alcohol withdrawal, one with cranial trauma, and two with low consciousness. Generalised convulsions were described in six and partial seizures with or without secondary generalisation in four. Six were classified as NORSE, one alcohol withdrawal, one fat embolism, one cranial trauma and one bleed of aneurysmal malformation. The duration of the SRSE ranged from 7 to 120 days. The EEG recording was performed with scalp electrodes, although some of them with needles due to skin lesions. The treatment provided included anti-epileptic drugs, general anaesthesia, magnesium, immunotherapy and hypothermia.
Outcome based on cerebral performance category (CPC) scale ranged from 1 to 5, 1 being good cerebral performance and 5 brain death. Three patients are back to their baseline, one with CPC 1 and two with CPC 2, two CPC 3, two CPC 4 and three CPC 5.

The three patients with favourable outcome had partial onset SRSE and the three that died generalised. The three deaths were associated to the main drug that suppressed the SRSE, thiopentone in two and midazolam in one.

**Conclusion:** Good outcome is possible after SRSE despite mortality rate being 50%. In our series, three patients had favourable outcome and three died which was directly associated to the main drug that could suppress the SRSE. Daily recorded EEG provided essential information to guide treatment. Benefits and risks of treatment should be considered as a potentially reversible cause of SRSE should always be treated.

**P30**

**Predicting refractoriness development in Status Epilepticus: a two-years prospective study**

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**Background:** Refractory Status Epilepticus (RSE) is a condition characterized by high short term morbidity and mortality. Many studies have focused their attention on the identification of the refractoriness predictors with different and sometimes contrasting results. Acute symptomatic aetiology and coma/stupor at first clinical evaluation are the most important and agreed predictors of Status Epilepticus (SE) refractoriness development. Moreover, the development of infections during the SE is another recently identified factor.

**Methods:** We aimed to define the predictors of refractoriness development in an adult cohort (≥ 14 years old) of patients diagnosed with SE prospectively collected at the Ospedale Civile Sant’Agostino Estense, Modena, Italy, during a two-years period (01-09-2013/31-08-2015).

**Results:** we observed 175 SE episodes occurring in 162 patients (98 females, 60.5%; age 14-94 years, mean 70). 37 patients (22.8%) had a RSE and among them 26 patients had a Super Refractory Status Epilepticus (SRSE). The RSE group had the highest 30-days morbidity (mean 30 days mRS score was 4.5 in RSE versus 3 in the responsive group) and 30-days mortality (43% versus 19% respectively). In the multivariate analysis the independent predictors of refractoriness were: age < 70 years (OR 3.20), development of infections during hospitalization (OR 4.49) and GCS ≤ 8 at SE onset (OR 13.76). The best predictive model showed a good accuracy for 30-days refractoriness prediction (AUROC 0.87).

**Conclusions:** we confirmed that RSE is a very severe condition, characterized by high short term morbidity and mortality. Younger patients and coma at the beginning of SE appear to be tightly related to an increased risk of refractoriness development probably due to a different etiologies distribution (severe etiologies such as post-anoxic are more represented while less severe etiologies such as cerebrovascular disease and remote symptomatic etiologies are less represented). Regarding infections, even if it is plausible that infections complications are the consequence of longer ICU stay and anesthetics use in RSE, it could also be that prolonged seizure activity is triggered and sustained by the systemic inflammatory reaction during infectious complications.

**P31**

**Risk score for drug-resistant epilepsy development after convulsive status epilepticus (DRESE)**

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**Background:** Although much attention has been paid to
mortality and disability of SE, none of published researches have addressed drug-resistant epilepsy (DRE) development in patients with SE, nor have its relevant predictors been investigated. Our aim is to develop a comprehensive prognostic score to promptly identify patients at high risk of DRE development after convulsive status epilepticus (CSE).

Methods: From May 2008 to September 2015, 139 consecutive patients identified with SE in a tertiary academic medical care center were reviewed. The patients were assessed according to diagnosis guidelines of DRE proposed by the International League Against Epilepsy (ILAE). Age, gender, history of epilepsy, Glasgow Coma Scale (GCS) on admission, and related clinical features were collected and analyzed using univariate and multivariate logistic model. A predictive score was developed with the independent predictors identified in the multivariate logistic model.

Results: After median observation time of 46 months, 90 patients were enrolled into this study. 39 (43.4%) patients were assessed as non-DRE, 19 (21.1%) were DRE, and 32 (35.6%) were deceased. History of epilepsy (OR, 15.16, 95% CI, 2.30-99.80, p=0.005), serum albumin <37g (OR, 7.15; 95%CI, 1.18-43.54; p=0.03), SE duration ≥ 24h (OR, 6.09; 95% CI, 1.23-30.26; p=0.03), apparent forebrain cortical or hippocampal abnormalities on neuro-imaging (OR, 7.31; 95% CI, 1.37-39.14; p=0.02) were independent predictors. A 9-point predictive model was built based on \( \beta \)-coefficients in the multivariate regression model, which we refer to as DRESE score. And the Hosmer-Lemeshow goodness of fit test had a p value of 0.695. The ROC analysis showed that the DRESE produced an excellent prediction of DRE development after CSE (AUC, 0.860; 95% CI, 76%-96%).

Conclusion: History of epilepsy, serum albumin <37g/L, SE duration ≥ 24h and apparent forebrain cortical or hippocampal abnormalities on neuro-imaging were independent predictors for DRE development in patients with CSE. With high accuracy, the DRESE is a great help for physicians to promptly identify and vigilantly monitor the patients at high risk of DRE development after CSE, and make better clinical intervention strategies.

P32 – BEST POSTER

Complication Burden Index (CBI) – a score for comprehensive evaluation of the effect of complications on functional outcome after status epilepticus

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Background: Systemic complications are common in status epilepticus (SE) and involve every organ system. Infection, vasopressor use and mechanical ventilation have been associated with poor outcome. However, we lack tools to evaluate total complication burden and its effects on outcome.

Methods: To comprehensively estimate burden of SE complications during treatment we created Complication Burden Index (CBI) by scoring the patient for 13 complication categories: respiratory, cardiovascular, nervous, renal, hepatic, coagulation, gastrointestinal and musculoskeletal systems, electrolyte/acid-base balance, infection, hypo-/hyperglycemia, skin/allergic reactions and mental condition. The categories were derived from ICU scoring systems SOFA, APACHE III, SAPS II and MODS supplemented with commonly encountered SE complications. Each category was scored only once regardless of the severity or the number of complications in that category. Thus, maximum CBI is 13. Relative Risk and ROC-Curve calculations were performed to assess optimal cut-off for predicting functional outcome. We internally validated the CBI in a retrospective material of 70 consecutive GCSE patients (≥16 years) treated in a tertiary hospital over a 2-year period. Outcome was defined as functional outcome at discharge using Glasgow Outcome Scale (GOS 1-3=poor vs. GOS>3=good) and condition relative to baseline condition (worse vs.
baseline). Association of the complications to functional outcome was obtained by univariate analysis.

**Results:** At discharge, functional outcome was poor (GOS1-3) in 40% and worse than baseline condition in 59%. In-hospital mortality was 7%. Average CBI was 3.8 (Range 0-10, Median 3). Optimal cut-off predicting poor functional outcome was >3 (GOS1-3 - RR 1.8, p=0.045, 95%CI 1.01-3.33; ROC-AUC 0.687, p=0.008, sensitivity 64%, specificity 61%), (Worse condition RR 1.52, p=0.04, 95%CI 1.02-2.26; ROC-AUC 0.662, p=0.022, sensitivity 56%, specificity 69%). Anesthesia, infections or mechanical ventilation were not significant predictors of functional outcome. Vasopressor use was associated with poor outcome (GOS1-3) p=0.018. CBI with cut-off >3 and as a continuous variable was associated with GOS1-3 (p=0.042, p=0.007) and with worse condition (p=0.041, p=0.022).

**Conclusions:** CBI is a novel tool for comprehensive management of SE complications relating to poor/worse functional outcome with cut-off >3. Although awaiting external validation, it may be useful in SE outcome studies as a prognostic marker.

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**P33**

**Outcome scores in non-hypoxic status epilepticus: EMSE and STESS in prospective comparison**


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**Background:** Status epilepticus (SE) is a potentially life threatening condition. Clinical scores may estimate risk of bad outcome in order to optimize treatment and patient allocation to intensive care unit or normal ward. SE severity Score (STESS) was the first score available. Epidemiology based Mortality Score for SE (EMSE) was published recently and will be evaluated prospectively in a multicenter study compared to STESS.

**Methods:** We investigated a total of 100 consecutive patients with non-hypoxic status epilepticus admitted to two centres, i.e. Mayo Clinic, Rochester, MN, and Salzburg, Austria. Inclusion criterion was status epilepticus lasting longer than five minutes with any semiology and an EEG within the first 24 hours. Patients had to be older than 18 years. All aetiologies were included, except cerebral hypoxia due to cardiac arrest. In STESS, risk assessment is based on level of consciousness before treatment, “worst” seizure type, history of previous seizures and age. In EMSE-EACE score, risk points are given for aetiology, age, comorbidity and EEG based on published mortality rates in epidemiological studies. STESS was applied with two cut-off values of 3 or 4 points indicating higher mortality risk when reaching or exceeding this value. Patients with 64 points or more in EMSE were regarded to have a higher risk of non-survival. ROC-curves were calculated for non-survival and clinical deterioration at discharge. The treating clinicians were blinded to result of score results in this non-interventional study.

**Results:** For the total study group, the area under the curve (AUC) of the ROC of EMSE (0.87 [0.80-0.94]) was higher than for STESS (0.76 [0.66-0.87]) concerning non-survival, but did not reach statistical significance (p=0.108). The AUC of the ROC of EMSE for predicting clinical worsening with EMSE (0.79 [0.7-0.89]) had a non-significant trend for superiority over STESS (0.74 [0.65-0.84]) with p=0.406.

**Conclusion:** EMSE and STESS do not differ in global performance in this study. However, patient population is a major determinant which score to use best in which centre.
**P34**

**Prognosis of poststroke status epilepticus (SE): differences according to timing between stroke and SE**

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**Introduction:** Prognosis in Status Epilepticus (SE) is related with etiology. Regarding post-stroke epilepsy, SE is infrequently reported and their consequences according to the timing of SE after stroke remains to be discussed. We aimed to investigate the outcome of patients with poststroke SE (PSE).

**Methods:** All SE patients in our center are prospectively collected in a database since February 2011; we selected all patients with stroke as etiology (ischemic and hemorrhagic). We assessed demographics, previous epilepsy, SE type, level of consciousness, mSTESS, SE duration, refractoriness, and type of stroke, location; regarding to outcome we collected the status at discharge and at last follow-up.

We evaluated 95 PSE: 54 ischemic and 41 hemorrhagic. 40 (42.1%) were female. Mean age: 72.7 ± 13.56. 33 (34.7%) had a previous history of epilepsy. 51 (53.7%) showed prominent motor symptoms. 49 (51.6%) needed > 2 AEDs and 27 (28.4%) anesthetics for their treatment. The median duration was 12 hours (4-48). Median time between stroke-SE was 15 days (0-532). Regarding the outcome at discharge, 34 patients (35.8%) fully recovered and the rest had a bad prognosis: 44 (46.3%) showed a functional decline and 17 (17.9%) died.

**Results:** At discharge, after a logistic regression, the occurrence of SE within the 72 hours after the stroke onset (p=0.003) and baseline mSTESS (p=0.010) were the only factors predicting mortality. Considering the functional decline, females (p=0.019), a low level of consciousness (p=0.051), timing between stroke-SE below 90 days (p=0.0001) and a SE duration >12 hours (p=0.011) remained as independent predictors for bad prognosis. We did not find any association with the type of SE or stroke.

At long-term follow-up (mean: 422 days), the occurrence of SE within the 72 hours after the stroke (p=0.0001) and baseline mSTESS (p=0.012) remained as mortality predictors, together with SE duration (p=0.004)

**Conclusions:** The timing of SE after stroke has different consequences in the patients with PSE: mortality was clearly increased within the first 72 hours after a stroke whilst a clinical decline remains more possible in the first 3 months. Other factors as mSTESS and SE duration affect not only outcome at discharge but also at long-term in PSE.

**P35**

**Risk score predictive of mortality in children with status epilepticus**

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**Background:** Children with status epilepticus (SE) are at higher risk of mortality compared with adults. This study aimed to develop and validate the risk score predictive of mortality in children with SE.

**Methods:** This study was a retrospective cohort. The inclusion criteria were patients aged under 18 years diagnosed as SE and treated between 2005 and 2015 all over Thailand. We retrospectively search eligible patients by using the ICD-10 code for SE; G41 on the national database of the Universal Health Coverage Insurance. Then, the outcome was death at discharge or within 30 days after discharge. All data were randomly divided into two groups; for model development and model validation. Factors associated death were analyzed by stepwise logistic regression analysis. The risk score was developed from the coefficients of variables in the final
logistic regression model. The final model was validated by comparing the area under receiver operator characteristic (ROC) curve for death of the model with another data set.

**Results:** There were 3,291 patients for model development, while 3,257 patients were used for model validation. The risk score based on model for death in children with SE was 4.5 x acute renal failure + 3.5 x heart diseases + 3.5 x shock + 3 x cancer + 2.5 x brain tumor + 1.5 x central nervous system (CNS) infection + 1 x anemia + 1 x congenital + 1 x septicemia. The risk score ranged between 0 and 21.5 with the cut point of 1 indicated high risk for death. The area under ROC curve for death of the final model was 74.88% (95% CI: 71.09 % – 78.67%) with sensitivity of 63.24% (95%CI: 61.59% – 64.88%) and specificity of 79.07 % (95%CI: 77.68% – 80.46%). The area under ROC curve of the model validation was 73.65% (95% CI: 69.67% – 77.63%) with sensitivity of 61.75% (95% CI: 60.08% – 63.42%) and the specificity of 74.93% (95%CI: 74.11% – 75.75%).

**Conclusion:** Based on the model, children with SE who had the risk score of one or more were high risk for death. Physicians should be aware of high mortality rate in these particular patients.

**P36**

**Risk score predictive of mortality in elderly patients with status epilepticus**

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**Background:** Elderly patients with status epilepticus (SE) are at higher risk of mortality compared with adults.

This study aimed to develop and validate the risk score predictive of mortality in elderly patients with SE.

**Methods:** This study was a retrospective cohort. The inclusion criteria were patients aged over 60 years diagnosed as SE and treated between 2005 and 2015 all over Thailand. We retrospectively search eligible patients by using the ICD-10 code for SE; G41 on the national database of the Universal Health Coverage Insurance. The outcome was death at discharge or within 30 days after discharge. All data were randomly divided into two groups; for model development and model validation. Factors associated death were analyzed by stepwise logistic regression analysis. The risk score was developed from the coefficients of variables in the final logistic regression model. The final model was validated by comparing the area under receiver operator characteristic (ROC) curve for death of the model with another data set.

**Results:** There were 2,304 patients for model development, while 2,302 patients were used for model validation. The risk score based on model for death in elderly patients with SE was 3.5 x septicemia + 3.5 x shock + 3.5 x central nervous system (CNS) infection + 2.5 x acute renal failure + 2 x chronic renal failure + 2 x heart diseases + 1.5 x respiratory failure + 1.5 x pneumonia + 1x anemia. The risk score ranged between 0 and 21 with the cut point of 2 indicated high risk for death. The area under ROC curve for death of the final model was 75.02% (95% CI: 73.00% – 77.04%) with sensitivity of 67.14% (95%CI: 65.22% – 69.05%) and specificity of 71.27% (95%CI: 69.43% – 73.12%). The area under ROC curve of the model validation 75.40% (95% CI: 73.32% – 77.48%) with sensitivity of 66.18% (95% CI: 64.25% – 68.11%) and the specificity was 74.19% (95%CI: 72.40% – 75.98%).

**Conclusion:** Based on the model, elderly patients with SE who had the risk score of two or more were high risk for death. Physicians should be aware of high mortality rate in these particular patients.
P37

Risk score predictive of mortality in status epilepticus

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Background: Status epilepticus (SE) is a serious neurological condition with high morbidity and mortality. This study aimed to develop and validate the risk score predictive of mortality in patients with SE.

Methods: This study was a retrospective cohort. The inclusion criteria were all patients diagnosed as SE and treated between 2005 and 2015 all over Thailand. We retrospectively search eligible patients by using the ICD-10 code for SE; G41 on the national database of the Universal Health Coverage Insurance. The outcome was death at discharge or within 30 days after discharge. All data were randomly divided into two groups; for model development and model validation. Factors associated death were analyzed by stepwise logistic regression analysis. The risk score was developed from the coefficients of variables in the final logistic regression model. The final model was validated by comparing the area under receiver operator characteristic (ROC) curve for death of the model with another data set.

Results: There were 10,924 patients for model development, while 10,808 patients were used for model validation. The risk score formula for death in SE was 5 x shock + 4 x age over 60 years old + 3.5 x heart diseases + 3 x acute renal failure + 3 x septicemia + 2.5 x central nervous system (CNS) infection + 2.5 x age 41-60 years old + 2 x cancer + 2 x chronic renal failure + 1.5 x age 21-40 years old + 1 x pneumonia + 1 x respiratory failure + 1 x anemia. The risk score ranged between 1 and 32 with the cut point of 4 indicated high risk for death. The area under ROC curve for death of the final model was 83.59% (95% CI: 82.51% – 84.67%) with sensitivity of 78.20% (95% CI: 77.42% – 78.97%) and specificity of 75.20% (95% CI: 74.57% – 76.19%). The area under ROC curve of the model validation was 83.52% (95% CI: 82.44% – 84.60%) with sensitivity of 77.87% (95% CI: 77.09% – 78.65%) and the specificity of 74.93% (95% CI: 74.11% – 75.75%).

Conclusion: Based on the model, patients with SE who had the risk score of four or more were high risk for death. Physicians should be aware of high mortality rate in these particular patients.

P38 – BEST POSTER

Which co-morbid conditions or complications of status epilepticus represent the highest risk for mortality?

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Background: Status epilepticus (SE) has high mortality rate; particularly those with co-morbid conditions or complications of SE. This study aimed to evaluate the highest risk for SE mortality in terms of co-morbid conditions or complications by using national database.

Methods: This study was a retrospective cohort design. The inclusion criteria were all patients diagnosed as SE and treated between 2005 and 2015 all over Thailand. We retrospectively search eligible patients by using the ICD-10 code for SE; G41 on the national database of the Universal Health Coverage Insurance. The outcome was
death at discharge or within 30 days after discharge. Cox proportional hazards regression was used to evaluate the association of co-morbid condition or complications of SE and mortality.

**Results:** During the study period, there were 21,732 eligible patients. The total observation time was 3,547.08 person-years with the median time of 6.34 years (95%CI: 5.06 – 8.38). The total mortality rate was 102.67 per 100 person-years (95%CI: 99.39 – 106.07) or 3,642 patients who died. The survival rates at 1, 3, 5, and 10 years were 58.1%, 54.6%, 52.5%, and 39.8% respectively. The co-morbid condition or complications positively associated with mortality were heart disease HR : 2.26 (95%CI : 2.08 – 2.46), shock HR : 1.90 (95%CI : 1.71 – 2.12), septicemia HR : 1.81 (95%CI : 1.67 – 1.96), acute renal failure HR : 1.75 (95%CI : 1.59 – 1.93), central nervous system infections HR : 1.74 (95%CI : 1.48 – 2.05), cancer HR : 1.57 (95%CI : 1.28 – 1.92), chronic renal failure HR: 1.56 (95%CI : 1.39 – 1.76), and respiratory failure HR : 1.48 (95%CI : 1.38 – 1.59).

**Conclusion:** Among several co-morbid condition or complications, heart disease was the highest risk factor for mortality in SE by national database.

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**CLINICAL INVESTIGATION**

**P39**

**Quantitative EEG interpretation by EEG-naive Neurointensivists before and after expert training**

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**Background:** Continuous and quantitative EEG (cEEG/QEEG) is a powerful monitoring tool for guiding diagnosis and therapy in the Neuro Intensive Care Unit (NICU), but its effective interpretation by non-Neurophysiologists is an unsettled issue. We evaluated the effect of a single cEEG/QEEG-focused training seminar on the interpretation skills of EEG-naive Neurointensivists in two distinct NICUs.

**Methods:** From 06/2015 to 09/2016, 35 Neurointensivists evaluated cEEG/QEEG tracings (350 before training; 86 after training) selected from patients admitted in the participating NICUs for different types of acute brain disorders. Four parameters were assessed: 1. depth of sedation, 2. asymmetry, 3. artifacts and 4. seizures. QEEG settings included density spectral array (DSA), amplitude-integrated EEG (aEEG), and burst-suppression rate (BSR). Data were collected using a web-based system. Answers given before and after training were compared with those of two expert Neurophysiologists, which performed the training seminar and represented the gold standard reference. Agreement was evaluated using Cohen’s Kappa.

**Results:** At baseline, sedation was correctly evaluated in 39.1%, asymmetry in 71.4%, artifacts in 40.6%, and seizures in 61.1% of tracings. K-values was poor for depth of sedation (0.06) and artifacts (0.08), fair for seizures (0.39), and moderate for asymmetry (0.46). After training, sedation was correctly recognized in 90.7%, asymmetry in 81.4%, artifacts in 95.3%, and seizures in 80.2% of cases. K-values of all parameters improved after training, particularly for depth of sedation (0.74) and artefacts (0.59), while a smaller effect was observed for asymmetry (0.63) and seizures (0.47).

**Conclusions:** A simple cEEG/QEEG-focused training was effective in improving detection rates by Neurointensivists of common phenomena in NICU patients monitored with cEEG/QEEG.
**Poster Abstracts**

**P40  – BEST POSTER**

**Electroencephalographic evaluation of benign patterns in patients with hypoxic ischaemic encephalopathy post cardiac arrest**

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**Background:** ‘Malignant’ EEG patterns, known for their poor outcome (1), have been extensively studied and defined in the literature. Consequently, an inevitable need has emerged to identify electroencephalographic activities in post cardiac arrest comatose patients that could be classified as ‘benign’ patterns and be associated with good outcome. We reviewed our database of cardiac arrest patients to identify and analyse these electroencephalographic features in patients who survived after cardiac arrest and did not show malignant patterns in their first EEG, as well as define their clinical profile.

**Methods:** All cardiac arrest patients treated at King’s College Hospital between 2010 and 2015 were identified. We included patients who were comatose survivors and did not show malignant patterns in their first EEG and were over 18 years of age. We collected clinical data including age, gender, downtime, cardiac arrest aetiology, EEG patterns, EEG reactivity, presence of seizures or myoclonus and outcome. Survivors were defined as patients who were discharged from hospital to home or neurorehabilitation unit. The relationship between the clinical variables, the EEGs and patients’ survival was evaluated retrospectively.

**Results:** 26 post cardiac arrest patients with benign patterns were identified and posteriorly divided and analysed into 2 subgroups: survivors (15/26) and non-survivors (11/26). The mean age of patients was 59.7±14.8 years old, with 20 male (77%) and 6 female (23%). There was no statistical significance when comparing clinical characteristics between survivors and non-survivors to demonstrate survival rate. Regarding the EEG patterns, significant statistical evidence for patients’ survival was found for reactivity (p = 0,028), presence of intermixed fast activity (p = 0,004) and the absence of epileptiform discharges (p = 0,015).

**Conclusions:** Post cardiac arrest EEG benign patterns, associated with good outcome, can be defined by the presence of reactivity, the presence of intermixed fast activity and the absence of epileptiform discharges, in addition to the absence of malignant patterns on their first EEG.

**P41**

**Periodic eye opening associated with EEG burst suppression following cardiac arrest. Is it all in the eyes?**

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**Background:** Eye opening is an important sign of wakefulness. This applies to clinical examination of the level of consciousness, including with structured assessments such as the Glasgow Coma Scale. An understanding of the relationship between the eyes and wakefulness also prevails more generally in society, influencing the perceptions of the relatives and carers of unconscious individuals. However, eye opening, which is likely mediated by a combination of midbrain and cortical mechanisms, can also be seen in pathological states where it may not be reflective of wakefulness.

**Case report:** We describe a case of recurrent eye opening as part of an unusual electro-clinical phenomenon. We present the case of a patient with hypoxic-ischaemic encephalopathy who developed periodic spells of eye opening 12 hours following in-hospital cardiac arrest. An electroencephalogram was urgently performed and this showed a burst-suppression pattern. Importantly, the bursts of activity on EEG were found to be time locked to the periods of eye opening. In the context of the case history, we characterise the temporal relationship between the clinical and electroencephalographic features. We relate our findings and the patient’s subsequent outcome to a small existing literature, and briefly review the underlying anatomy and physiology.
Discussion: We discuss the importance of recognising and understanding the significance of this rare but striking clinical sign. We argue that such an understanding can provide additional guidance for clinicians as well as patients’ relatives when navigating the challenging clinical and ethical questions surrounding the care of patients who have suffered hypoxic brain damage following cardiac arrest.

P42

Generalized periodic discharges characteristics and outcome in post cardiac arrest

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Background: The neurophysiological findings of generalized periodic discharges (GPDs) are generally recognized as “malignant” pattern in cardiac-arrest survivors. However, their predictive role is controversial. The American Clinical Neurophysiology Society standardized the terminology of periodic patterns. The aim of this study is to evaluate the association between GPDs major and minor modifiers and outcome at hospital discharge in comatose post-cardiac arrest patients.

Methods: we retrospectively collected clinical and electrophysiological data of adult patients (≥18 yrs old) admitted at the King’s College Hospital from 1st January 2010 to 31st March 2016 with in- or out of the hospital cardiac arrest who underwent at least one EEG and this showed GPD pattern. ACNS terminology was used to characterize GPD patterns and appropriate statistical analysis were performed to identify clinical and electrophysiological elements associated with outcome.

Results: 36 out of 234 patients had a GPD pattern: 16 patients survived and were discharged from the hospital. Statistical analysis showed significant correlation between survival and a low to normal background voltage, theta background rhythm, background reactivity to external stimuli, low to normal GPD interdischarge voltage, sharp or blunt morphology and no GPD evolution. Interestingly, response to BDZ was associated with greater mortality.

Conclusions: Different intrinsic characteristics of generalized periodic patterns may predict survival in post-cardiac arrest patients. ACNS standardized terminology is a useful tool for a better characterization of GPD patterns and its use is highly recommended. Further prospective and multicentre data are needed to validate our findings.

P43

Which is the adequate ketamine EEG pattern to control status epilepticus?


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Objective: The aim of the study is to describe the EEG changes produced by Ketamine (KET) in patients with superefractory Status Epilepticus (SRSE).

Methods: We retrospectively analyzed the data of patients with SRSE treated with KET alone (without other anesthetics at coma dosis) in the Intensive Care Unit, Hospital de Bellvitge, Spain, from 2008 to 2016. Data collection included demographic features, clinical presentation, diagnosis, continuous video-electroencephalogram (cEEG) data, treatment with KET: duration, effect of loading dose and maintenance dose on Seizure control and on cEEG and side effects. Outcomes were seizure control, status control and death.

Results: 6 patients with SRSE were treated with KET of them, 2 patients were excluded. One patients because no cEEG was done during the KET treatment and the other patient was excluded because KET did not produce EEG changes (the dose administrated was low, less that 100 mgr per day). Finally 4 patients were included, 2 women (50%)(mean age 51.2). Prior to KET the patients received a median of three anesthetistic comas and five iv-antiepileptic drug. One patient received several bolus of KET (up to 250mgr) followed by a continuous infusion and
the others a continuous infusion directly. Mean duration of KET coma was 13 days (7-17), mean total daily dose 4875 mg (3500-6000). The EEG changes induced by KET was continuous EEG with generalized frontally predominant beta rhythm superimposed with delta rhythm. Seizures were controlled for > 24 hours in all, 4/4 (100%). Interictal epileptiform discharges (IED) disappeared in 3/4 (75%). KET coma controlled the status in 2/4 (50%). Overall mortality was 1/4 (25%).

**Conclusion:** KET does not induce a burst suppression pattern. KET bolus is extremely fast in controlling seizures. The desired KET coma pattern is a continuous EEG with a generalized frontally predominant beta rhythm superimposed with delta rhythm and without IED.

**P44 – BEST POSTER**

**Status epilepticus related acute MRI alterations in an adult population: definition of MRI findings and clinical-EEG correlation**

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**Background:** Magnetic resonance imaging (MRI) provides an opportunity for identifying early seizure related neuronal damage. Sustained electrical activity can cause extremely variable MRI alterations, in different cerebral areas that are generally completely reversible. These alterations are well known, however, reports in literature are scares and based mainly on small selected populations.

**Methods:** Retrospective monocentric study on an adult Status Epilepticus (SE) population studied with a brain MRI in the acute/subacute phases of SE in Department Neurology, Christian Doppler Klinik, Paracelsus Medical University, Salzburg, Austria during a 5-year period (01.01.2011 – 31.12.2015). The inclusion criteria were: 1) An electro-clinical diagnosis of SE, 2) an MRI performed within 30 days from the beginning of SE.

**Results:** We identified 277 patients fulfilling the selection criteria (58% males, mean age of 63 years; range 13 - 90 years). Among them, 32 (12%) were judged having an acute / subacute MRI changes related to SE. The most important risk factor for the appearance of SE-related MRI alterations was the duration of SE: mean duration of 6 days versus 2 days (p = 0.011) respectively in the group with and without MRI alterations while they did not differ for gender, age, etiologies distribution and response to treatment. Focal abnormalities on EEG (p = 0.00003) and in particular, Lateralized Periodic Discharges (LPDs) (p < 0.0001) were strongly associated with SE related MRI alterations. These were unilateral (23 patients, 72%), located in multiple brain structures (19 patients, 59%) involving mesio-temporal structures (17 patients, 53%). 16 patients (50%) presented an almost perfect correspondence between MRI local alterations and focal pattern on EEG; moreover 12 patients (38%) had focal activity on EEG and MRI changes involving, at the same time, either local structures corresponding to the site of the highest EEG activity or the deep structures. On follow-up in 71% of the patients the MRI’s alterations were completely disappeared.

**Conclusions:** The MRI performed in the acute/subacute phase of SE helps better defining the structures and the spreading pattern of ictal activity involved during the different phases of the SE.

**P45**

**Usefulness of dynamic brain perfusion CT in status epilepticus**

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**Background:** Perfusion CT (P-CT) is an available tool in most emergency departments that can measure cerebral blood perfusion, and it is known that perfusion can be used for localizing the epileptogenic zone. The utility of Perfusion CT (P-CT) in SE is based exclusively on a very few retrospective analysis, so our aim was to evaluate the diagnostic value of perfusion CT (P-CT) in SE.

**Methods:** We conducted a prospective study in which 21 consecutive patients with SE (17 with NCSE confirmed by EEG and 4 patients with clinically witnessed prolonged seizures) were performed P-CT in this acute setting. Visual analysis of the perfusion maps was performed. For the quantitative assessment, the regions of interest (ROIs) were analysed at the locations that the maps suggested alterations and were compared with a corresponding region in the unaffected cortical region of the other hemisphere.

Asymmetry indices between affected and unaffected hemispheres were calculated for regional cerebral blood flow (rCBF), regional cerebral blood volume (rCBV), time to peak (TTP) and mean transit time (MTT).

Regional perfusion changes were compared to EEG findings, and clinical symptoms

**Results:** We included 18 patients. Mean age: 70.2 ± 16.1[25-90]. 72.2% were male. 2 patients was excluded due to bilateral EEG alteration and 1 for incomplete data.

Regional cortical hyperperfusion was depicted in 16/18 (88.9%) of patients with SE by analysis of parametric perfusion maps during emergency conditions. The areas of hyperperfusion were concordant with transient clinical symptoms and EEG topography in these cases.

Quantitative analysis showed a significantly increased regional cerebral blood flow (p=0.002), increased regional cerebral blood volume (p=0.004), decreased in time to peak (p<0.001) and decreased in mean transit time (p=0.001). The mean asymmetry index was 12.9 in rCBF; 14.0 in rCBV; -3.1 in TTP and -3.7 in MMT.

**Conclusion:** Visual and quantitative analysis of perfusion maps detected regional hyperperfusion in SE in 88.9% of patients. Significant alterations were observed in rCBF, rCBV, TTP and MMT so the use of P-CT in SE may accelerate the diagnosis and may qualify as a complementary diagnostic to EEG.

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**Elevated CSF TRAIL level distinguishes viral meningoencephalitis from autoimmune encephalitis at early phase in the epileptogenesis of TLE**

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**Background:** Autoimmune encephalitis (AE) is a diverse group of neuro-psychiatric disorders recognized recently, which can be treated with immune modulating therapies such as steroids, intravenous immunoglobulins, and others. Distinguishing AE from infectious meningoencephalitis at early phase is very important because each of them requires different type of treatments. However, AE and viral meningoencephalitis (VME) can present with similar symptom at the early phase of the disease. The elevated blood level of a protein called TNF-related apoptosis-inducing ligand (TRAIL) has been reported to be useful for distinguishing viral infection from bacterial infection or non-infectious patients. Here, we investigated if the CSF TRAIL level can be useful for distinguishing viral meningoencephalitis from autoimmune encephalitis or non-infectious neurological disorders.

**Methods:** A total of 30 patients were included in the analysis. Ten patients were diagnosed as autoimmune encephalitis (AE) supported by autoantibody detection, 5 Anti-N-methyl D-aspartate receptor (NMDAR) encephalitis and 5 Anti-leucine rich glioma inactivated 1 (LGII1) encephalitis; 10 patients were confirmed as viral meningoencephalitis (VME) by cerebrospinal fluid (CSF) PCR, 5 Japanese encephalitis virus (JEV) and 5 Herpesviridae; and 10 patients were non-infectious neurological patients, including dizziness, orthostatic hypotension, and vasovagal syncope. CSF was obtained from the patients before the initiation of any treatment and were stored in - 80°C. CSF TRAIL levels were measured by ELISA (R&D system).
Results: The CSF TRAIL level in the VME group was elevated to 49.4±18.8 (mean±SEM) while those in AE and control group were 5.1±1.0 and 2.0±0.6, respectively. When the optimal cut-off value was selected, the sensitivity and specificity for detecting VME from total patients were 90% and 95%, respectively. On receiver operating characteristic (ROC) curve analysis, the area under curve (AUC) was 0.975. Among the 20 encephalitis patients, sensitivity and specificity for detecting VME were all 90%, and the AUC was 0.950.

Conclusions: Our result demonstrates that CSF TRAIL level can be used for distinguishing VME patient from AE or other neurological diseases at early phase. This can be extremely useful in the clinical practice for helping the physicians to make an early decision of proper treatment for the encephalitis patients.

P47

Erythropoetin, Interleukin-6 and Progranulin as markers of neuronal repair and neuroinflammation in the cerebro spinal fluid of status epilepticus patients

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Background: Data on repair mechanisms after status epilepticus (SE) scarce. Cerebro Spinal Fluid (CSF) elucidate pathomechanisms and especially repair mechanisms initiated after SE give insight into neuroimmunological mechanisms.

Methods: We retrospectively CSF samples of patients and with other neurological diseases (e.g headache). Samples were taken workup. We measured rogranulin (PGRN) as a marker inflammation and/or repair (n=21 SE patients), rterleukin-6 (II-6) as marker of acute inflammation (n=22 SE patients) and rythropetin (EPO) as a marker hypoxemia (n=31 SE patients) measurements were performed with commercial ELISA system statistics were done via SPSS 22.0. We also our SE-patients into three groups on time between lumbar puncture and end of the SE (0-24hours, 24-48hours and 48+ hours). We excluded patients with encephalitis or cerebral/myocardial ischemia from Il-6 statistics elevated Il-6 levels in these patients. Furthermore, the blood-brain leakage (Qalb) was calculated for every patient.

Results: PGRN and Il-6 were significantly higher across the whole cohort Il-6 levels showed a wide range from 0.00-251.3 [pg/ml]. There wcorrelation between EPO and Il-6 (Pearsons Correlation r=-0.16) or EPO and PGRN (r=-0.139). he interrelation between Il-6 and PGRN revealed a highly significant correlation (r=0.91 and p<0.001). Student’s t-test showed a strong tendency for a decrease of EPO CSF-levels 24+hours after SE (p=0.056). Qalb was slightly pathological showing a discrete blood brain leakage at all timespans.

Conclusions: Elevated PGRN-levels he decrease of EPO be a sign of an acute reaction to hypox. This explain decrease after 24-48 hours.

P48

The long-term risk of new onset epilepsy in critically-ill patients with periodic discharges on continuous EEG monitoring

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Background: Widespread use of continuous EEG (cEEG) monitoring has led to frequent findings of periodic discharges in the critically ill patients, which have varying degree of association with seizures in acute setting. However, their association with development of epilepsy after resolution of acute insult has not been described. This is the aim of our study.

Methods: Our cEEG database from 01/01/2013 to 06/30/2013 was reviewed to find patients fulfilling
following criteria: age \( \geq 18 \) years, no epilepsy history, periodic discharges [Lateralized (LPDs) or Generalized (GPDs)] or non-epileptogenic findings on cEEG and at least 3 months clinical follow-up. Medical records were reviewed. A chi-square test of the individual independent variable followed by construction of a multivariable logistic regression model using the statistically significant variables (\( p<0.05 \)) was performed. Clinical seizures after discharge was the primary outcome.

**Results:** A total of 226 patients with 126 (55.8%) women and average age of 66.3 (+/-13.5) years were studied. Seventy one (31.4%) had LPDs, 79 (35%) GPDs and 76 (33.6%) had non-epileptogenic findings on cEEG. Thirty one (43.7%) patients with LPDs had concomitant electrographic seizures on cEEG compared to 9 (11.4%) patients with GPDs. Structural brain lesion was etiology in 151 (66.8%) patients and most common among patients with LPDs (84.5%). A total of 37 (16.4%) patients [LPDs = 28 (39.4%), GPDs = 6 (7.6%), non-epileptogenic = 3 (3.9%)] developed clinical seizures after discharge during a median follow-up period of 2.6 (0.25 – 4) years. Etiology (structural lesions), cEEG findings, electrographic seizure and AED at discharge were significantly associated with primary outcome on univariate analysis and were included in the final model. Presence of LPDs [Odds ratio (OR) = 4.2 (1.6 – 10.6)] and electrographic seizures [OR = 2.7 (1.1 – 6.6)] were the only variable predictive of primary outcome (\( p<0.0001 \)).

**Conclusions:** While LPDs and electrographic seizure noted on cEEG independently predict the long term risk of epilepsy development, the risk is not as high with GPDs, which may be secondary to etiology. Our retrospective study shows that the utility of cEEG can be expanded beyond acute management to help predict patients at high risk of development of epilepsy.

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### P49

**QuoStatus: a software package for the analysis of the intensity and progression of status epilepticus in EEG signals**

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**Background:** Research aimed at developing new approaches to suppress status epilepticus (SE) would potentially benefit from automated and standardized approaches for analyzing the underlying electrical activity associated with SE. In this abstract and poster, we present QuoStatus, a free, user friendly, open-source, software program for the post-hoc analysis of the intensity and progression of SE in electrophysiological recordings (e.g., EEG). This software has been useful for the assessment of the efficacy of anti-seizure drugs.

**Methods:** QuoStatus computes the relative changes compared to baseline of three time-dependent variables for each electrophysiological recording channel submitted for analysis: (1) the change in power in a given frequency band; (2) the change in coastline length of the EEG; and (3) the change in spike frequency of the EEG.

**Results:** The program analyzes the intensity of the underlying electrical activity of SE and how it progresses by measuring these time-dependent variables every 15 min for up to 48 hr after the onset of SE. It can compare up to six experimental cohorts, which for example could be the relative effects of six different drug dosages. It then computes the time-dependent mean and 95% confidence intervals of all recordings within a cohort, as well as determining statistical significance between the means of all cohorts at every time interval. It produces both colour and greyscale publication-quality graphs in png, jpg and pdf format as output, with full control over line thickness, fonts, and captions, as well as saving all of the raw analysis results in Excel format.
Conclusions: QuoStatus can analyze Biopaq Acqknowledge (.acq) files, Cambridge Electronic Design spike2 (.smr) files and European Data Format (.edf) files, plus other file formats can be included on request. It has a simple installation program, will run on all major operating systems, is written in Python 2.7 and QT, and is released as freeware under the GNU GPL 3.0 software license. Its source code and underlying algorithms are available. Supported by the CounterACT Program, NIH Office of the Director and NINDS though an Interagency Agreement with the DoD.

P50

Electroencephalograhic patterns in nonconvulsive status epilepticus – associations with etiology and efficacy of antiepileptic drugs

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Background: In 2015 the ILAE launched a new status epilepticus (SE) classification system [1] based on four axes with electroencephalograhic patterns resembling axis 3. It was acknowledged that there were until then no specific electroencephalograhic patterns associated with a certain subtype of SE. This study was performed see whether there might be specific electroencephalograhic patterns associated with certain subtypes of nonconvulsive SE (NCSE) according to axis 1 (semiology) or axis 2 (etiology) of the new classification, or whether electroencephalograhic patterns are associated with efficacy of certain antiepileptic drugs.

Methods: In a retrospective databank analysis all treatment episodes of a NCSE between January 2010 and June 2013 in the department of Neurology at Rostock University were identified. The first EEG of each treatment episode, in which an EEG was recorded, was evaluated. Statistical analyses were performed in order to find out whether there is an association of a certain EEG pattern with a particular subtype of SE or whether some EEG patterns signify better efficacy of a certain antiepileptic drug in this condition.

Results: In 64 treatment episodes of a NCSE at least one EEG was obtained during the actual treatment. There was no association of a certain EEG pattern with a particular subtype of NCSE according to axis 1. But background slowing with a frequency in the theta-range or lower was more frequent in episodes with an acute (p < 0.00000001) or progressive etiology (p < 0.0000001) than in episodes with remote etiology (axis 2). In the 10 treatment episodes with generalized epileptiform activity among the four antiepileptic drugs Phenytoin, Valproate, Levetiracetam and Lacosamide only Levetiracetam was effective in at least one treatment episode. After Yates-correction for small sample size this yielded only a significant superiority to Valproate (p < 0.04). There were no other significant associations of electroencephalograhic patterns with the efficacy of a certain antiepileptic drug.

Conclusion: The concept of different subtypes of NCSE needs further evaluation especially with regard to its therapeutic relevance.


P51

Diagnostic yield of emergent EEG in patients with acute altered mental status

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Background: Non convulsive status epilepticus is a common acute neurological emergency that should be considered in the differential diagnosis of unexplained coma and confusional states. Emergent or continuous video EEG monitoring is required to diagnose and manage this entity; however, its availability during non-business hours is still scarce in many medical centers in our country.
Methods: We performed a retrospective review of patients who underwent emergent electroencephalography (eEEG) between February 1, 2016, and May 31, 2016, for an indication of altered mental status (AMS). In our center, the time response for an eEEG is under 3 hours. The EEGs and reports were reviewed for ictal activity, periodic discharges, interictal epileptiform abnormalities, and nonepileptiform abnormalities. Demographic and clinical data were gathered from the electronic medical record to determine seizure predictors.

Results: We performed 188 eEEG in patients with altered mental status, 79 of them during non-business hours. Status epilepticus was diagnosed in 22 (11.7%), of whom 10 were patients in coma. Seizures occurred in 8 (4.2%), epileptiform activity within the ictal-interictal continuum occurred in 4 (2.1%), clearly interictal periodic discharges in 8 (4.2%), de novo epileptiform activity in 17 (9%), and focal slowing without a known lesion in 16 (8.5%).

Conclusion: This study confirms the value of eEEG for the evaluation of altered mental status. Non convulsive status epilepticus and electrographic seizures occurred at a high frequency in this population. The eEEG contributed to the diagnosis in 39.7% of the cases, confirming the diagnosis of Status Epilepticus in 11.7%, and providing relevant information in an additional 28%.

PAEDIATRICS

P52

Hypsarrhythmia in infantile spasms is a highly synchronized state

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Methods: Nineteen channel Scalp EEGs with the 10-20 system of electrode placement for extraction of 10 second artifact-free epochs (n=10) in stage II non-rapid eye movement sleep. R-Index of synchronization calculated with the Laplacian estimate followed by the Hilbert Transform and the spatial complexity of R-Index ascertained at 3, 6, 11 and 15 Hz for comparisons with student T-test.

Results: Patient A: 6 month old male with genetic/metabolic disorder, MRI with delay in myelination [R-Index (Mean ± SD)= Hypsarrhythmia (13.4 ± 2.2); EDR (13.8 ± 2.1) p < 0.001]. Patient B: 15 month old male with global developmental delay, MRI showed prominence of extra-axial cerebrospinal fluid (CSF) in the anterior temporal, perisylvian and frontal regions [R-Index= Hypsarrhythmia (15.3 ± 1.7); EDR (14.8 ± 1.5) (p < 0.001)]. Patient C: 4 month old female with no EDRs on the EEG, MRI showed a remote infarct in the distribution of the right middle cerebral artery. Hypsarrhythmia (patients A and B) had...
higher R- Indices at the 3 Hz band only, compared to EDRs. The comparison of R- index of bilateral hypsarrhythmia vs. hemi-hypsarrhythmia (Patient C) showed no difference at the delta band (3 Hz). The alpha (10 Hz) and beta band (15 Hz) of patient C showed higher R- Index over the right middle and posterior temporal (T4 and T6) and right temporal-parietal (T4-P4) areas.

Conclusion: Hypsarrhythmia is a highly synchronized EEG pattern compared to the electrodecremental response. Stroke likely disrupts neuronal networks leading to hemi-hypsarrhythmia with higher ipsilateral R- Index of synchronization, consistent with non-convulsive status epilepticus.

P53

Early ictal and interictal patterns in FIRES patients: a single center case series

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Background: Febrile Infection-related Epilepsy Syndrome (FIRES) is a catastrophic epileptic encephalopathy described as explosive onset of super refractory status epilepticus (SRSE) in previously healthy children. The condition is one of exclusion and lacks biomarkers to facilitate a timely diagnosis. We describe EEG findings in the hyperacute phase of FIRES.

Methods: This is a retrospective single-center case series of seven children with FIRES. Patient characteristics and clinical course were obtained from electronic medical records. In this analysis, EEG review included the initial 12 hours and the 12 hours prior to initiation of medically induced burst suppression (BS).

Results: New onset seizure was the presenting symptom in all patients. There was gradual evolution to SRSE in all. In the first 12 hours of EEG, interictal features included generalized slowing in all and focal slowing in half. Sleep architecture was seen in only one EEG and all lacked a posterior basic rhythm. Delta brush (DB) was appreciated in 5 patients. Seizures in this period had focal onset, were brief and self-resolving. Electrographic seizures had characteristic appearance with abundance of fast activity and polyspikes. Average seizure duration was <5 minutes and average seizure burden was <1/hour with most patients having 0-5 seizures per 12 hour recording. No patient had status epilepticus (SE) at this stage.

Interictal EEG features 12 hours prior to BS included: diffuse slowing, absence of sleep architecture and posterior basic rhythm in all patients. Four patients had delta brush, not previously seen in 1 patient. Average seizure frequency was 3/hour with average duration of 5 minutes. All patients met criteria for electrographic SE, 2 had a continuous seizure > 30 minutes duration. Average time between the first and second EEG recording was 71 hours (range 12-160 hours).

Conclusions: We describe the hyperacute phase of FIRES. EEG characteristics included marked generalized slowing in all and DB in most. All patients had brief recurrent seizures with characteristic morphology. Seizures increased over several hours to days, ultimately progressing to SRSE. The seizure presentation and EEG features of FIRES appear rather uniform. Recognition of this pattern may facilitate early diagnosis and treatment. Additional studies are necessary to validate these findings.

P54

Consensus research priorities for paediatric status epilepticus: a Delphi study of consumers, researchers and clinicians

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mortality. Emergency physicians and neurologists are key stakeholders in managing this condition. Recommendations beyond first line care are based on expert opinion and non-experimental evidence. A collaborative, widely consulted, systematic approach to identifying immediate research priorities in SE is required to ensure limited research funds are directed appropriately. The objectives of this study are to identify consensus research priorities in paediatric status epilepticus among exerts and consumers.

Methods: A three-stage Delphi process was conducted. Paediatric Neurologists and Emergency Physicians in Australia and New Zealand were invited to participate by e-mail, and completed a specifically designed on-line survey. Round one asked participants to generate up to three research questions considered the most important regarding paediatric status epilepticus. Responses were collated and refined into unique individual questions. Rounds two and three required participants to rate each question on a seven point likert-type ordinal scale from 1 to 7 (very low priority to very high priority). Consumers were also invited to provide up to three problem areas that could/should be addressed by research.

Results: Fifty-four experts and 76 consumers participated in the process. Nine questions reached our definition of consensus “high priority”, 21 questions achieved consensus “low priority” and seven questions did not achieve consensus (intermediate priority). High priority areas included second line management including leviteracetam (efficacy, dose and timing), induction of anaesthesia (timing and best agent), and recognition of subtle SE. Consumer priority areas included broad themes of treatment efficacy, aetiology and community education.

Significance: We identified 9 priority research questions in paediatric SE, congruent with consumer priority theme of treatment efficacy. Involving emergency physicians, neurologists and consumers in the process is likely to facilitate research efforts with greater participation and buy in from clinicians, and assist with knowledge translation efforts.

P55

Efficiency and safety of levetiracetam in children with electrical status epilepticus of slow sleep (ESES) on the EEG

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Background: Electrical status epilepticus of slow sleep is an EEG pattern of continuous (85-100%) diffuse epileptiform activity on the sleep EEG. The morphology of epileptiform complexes is identical to benign epileptiform discharges of childhood (BEDC). Epilepsy with ESES (or “Penelope Syndrome”) is a form of age-dependent epileptic encephalopathies with the phenomenon of continuous spike-waves during slow wave sleep. This group of epilepsies also includes Pseudo-Lennox syndrome, Landau-Kleffner syndrome, autistic epileptiform regression and some others. ESES pattern is correlated with the severity of cognitive deficit in this population of epileptic children. The aim of this study was to evaluate the efficiency and safety of levetiracetam indicated to the children with ESES pattern on the EEG.

Subjects and Methods: During the period of 2010-2016 34 epileptic children with ESES on the EEG (14 boys and 20 girls) receiving levetiracetam (33 in combined and 1 in monotherapy) were observed.

Results: Patients with ESES on the sleep EEG were diagnosed the following forms of epilepsy: epilepsy with ESES – 28 cases (7 idiopathic, 13 symptomatic and 8 “symptomatic” cases of ESES resulted from “double pathology” of idiopathic + hypoxic-ischemic factors and these children had cerebral palsy), 3 cases of Pseudo-Lennox syndrome, 2 cases of Landau-Kleffner syndrome and one girl with autistic epileptiform regression. All presented children received levetiracetam in therapeutic doses 20-80 mg/kg/daily. Levetiracetam was highly effective in 67.6% of patients (n=23) – 2 cases demonstrated complex clinical and electroencephalographic remission
before puberty, 9 cases had clinical remission and 12 cases significant decrease of seizures and epileptiform discharges. Low efficiency was seen in 20.6% (n=7) patients. The aggravation effect has been noted in 11.8% (n=4) of patients. Other negative effects were observed in only 4 (11.8%) children (3 cases of agitation and sleep disturbance and allergic rush in one).

Conclusion: Levetiracetam is highly effective medication (67.6% of cases) in combined AED’s therapy of epilepsies with ESES. However, aggravation risk was as high as 11.8%. The most effective levetiracetam combinations were with valproates and ethosuximide.

P56

Diurnal variation of febrile seizures in Korean children

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Background: Febrile seizures are the most common type of seizure disorders in children. The aim of this study is to understand the diurnal variation of febrile seizures in Korean children by analyzing the differences in frequency, pattern and severity according to time.

Methods: This is a prospective single-centered specialized questionnaire-based study. Three hundred and sixty-two children diagnosed with febrile seizure from May, 2011 to May, 2013 in a referral center, Fatima Hospital, were involved. We evaluate the diurnal occurrence of febrile seizures for age, sex, temperature, time of occurrence, duration, type, and family history.

Results: Febrile seizures occurred more in the afternoon. The incidence of febrile seizures between 2 pm and 6 pm (group II) was approximately three times more (P=0.001) than that of between 2 am and 6 am (group I). The distribution curve revealed that the peak occurrence of febrile seizures was between 4 pm and 5 pm. The proportion of patients with body temperature over 40°C was significantly higher in group II than group I (P =0.03). There was no statistically significant difference for temperature, duration and type of seizures between two groups.

Conclusion: Febrile seizures showed diurnal change in the frequency of occurrence. They seem to occur in the afternoon more frequently when the set point of body temperature is elevated physiologically. Although the property and severity of febrile seizure was not altered by circadian rhythm of body temperature, its diurnal change in the frequency of occurrence might be attributable to a change in the thermoregulatory set point.

Keywords: Febrile seizure, Diurnal variation, Circadian rhythm, Child

P57

A narrative systematic review on the quality of life of families using the ketogenic diet for children with intractable epilepsy


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Background: The ketogenic diet (KD) has moderate to high success in reducing epileptic seizures in pediatric patients who are unresponsive to drug therapy. Metabolic ketosis is induced by altering dietary intake to high fat and low carbohydrate/protein components. The diet must be strictly followed to maintain ketosis. Little is known about the quality of life (QoL) for families maintaining this diet. We conducted a systematic narrative review to examine the quality of life for families with a child using the KD for reduction of seizures.

**Results:** Few measures of QoL were used in studies on the KD. Recurring themes included nutrition, growth and development, and psychosocial impact of the diet. Micronutrient deficiencies occur and children may not reach growth standards for their age but catch up growth occurs upon cessation of the diet. The dominant psychological factors included reduced sleep, and increased cognitive functioning which persisted after the diet was stopped. None of the studies mentioned specific counselling given to families on expected outcomes. Non-adherence and drop-out from studies were not well documented.

**Conclusion:** We think that given the success rates of decreasing seizure activity and the positive psychosocial outcomes, the KD could be offered as a first or second line treatment for epilepsy. The effect of the KD on QoL is unknown but we believe seizure reduction in children is a primary parental concern. The KD requires perseverance and effort. Simple checklists empower patients and their families, and increase adherence to treatment and self-management. We drafted a Family Checklist for Children on the Ketogenic Diet to use as an education guide for parents and health care providers. The Family Checklist is to be used as an education tool by healthcare practitioners and by families to mark changes in seven criteria of children whose parents and practitioners subscribe to the KD. Our next step is to pilot The Checklist.

**P58**

**Paediatric status epilepticus: identification of prognostic factors using the new ILAE classification**

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**Background:** Status Epilepticus (SE) is the commonest neurological emergency in childhood. Aim of this study is to report the characteristics of paediatric patients suffering from Status Epilepticus (SE) and their outcome with some considerations to the new classification issued by the International League Against Epilepsy (ILAE) in 2015.

**Method:** We included 173 children treated at “Bambino Gesù” Children’s Hospital in Rome (4.35±4.85 years old; follow up 2.74±1.9 years). Multivariate model was constructed to predict neurocognitive outcome, recurrence of SE, development of epilepsy and mortality. Adjusted ORs were calculated with 95% Confidence interval (OR[95%CI]).

**Results:** We observed a different prevalence of aetiologies for the different semioologies (p <0.05) and for each age-group (p <0.05), overlapping only in part with the recent ILAE classification. After SE, patients developed: 70% epilepsy (drug-resistant in half of them); 20% worsening of neurological exam; 16% cognitive deficit; 16% recurrent SE. At multivariate analysis: SE lasting more than 24 hours have increased risk to develop cognitive (OR=6.00[2.0-17.1]) or neurologic sequelae (OR=8.58[2.7-27.1]); the same finding was observed for patient younger than 1 months (cognitive OR=4.84[1.13-17.3] and neurologic sequelae OR 6.7[1.17-27.1]). The recurrence of SE was associated with genetic (OR=8.87[2.46-42.63]) and cryptogenic aetiology (OR=11.5[2.2-61.8]), as like myoclonic semiology (OR=6.1[1.1-29.4]). Febrile SE (OR=0.06[0.008-0.40]) and acute symptomatic aetiology (OR=0.12[0.04-0.40]) have a diminished risk to develop epilepsy. Drug-resistant epilepsy post SE was less frequent in focal non-convulsive SE (OR=0.18[0.32-0.97]) and acute symptomatic SE (OR=0.04[0.007-0.26]).

**Conclusion:** Age at onset and duration of SE are critical independent variables associated to worst neurocognitive outcome. The risk to develop epilepsy is lower after acute symptomatic and febrile SE. Semiology and age of onset are useful to predict aetiology of SE. For this reason, ILAE classification respect the 4 axes seems to be a good step forward.
**TREATMENT STUDIES**

**P59**

Towards a new way of managing refractory status epilepticus


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**Background:** Pharmacologically-induced coma targeting EEG burst suppression, at a level of “one burst per 10 seconds”, is standard treatment for refractory status epilepticus (RSE). Current management practices require manual titration of anesthetics over days. We hypothesized that 1) manual titration often fails to maintain clinically targeted levels of burst suppression, and 2) closed loop control technology can achieve better performance.

We demonstrate in silico and in animal studies that a physiological closed-loop control system (PCLCS), which adjusts the infusion rates based on the EEG in real time, maintains the desired level of burst suppression more accurately.

**Methods:** We quantified burst suppression over time in 35 patients treated with anesthetics for RSE. The clinical target was one burst per 10 seconds. Quantitatively, this objective means maintaining the burst suppression probability (BSP) – a measure ranging from 0 (no burst suppression) to 1 (isoelectric) – between 0.8 +/- 0.15. We measured the percentage of time in which the BSP was above (aPT), within (iPT) and below (bPT) the target range. Next, we designed a PCLCS to maintain BSP at 0.8 +/- 0.15 for 47 computer simulations of RSE patients, and in 2 rodents. In these experiments we tested robustness of control by applying disturbances in the form of sinusoidally varying extra sources of propofol to mimic pharmacodynamic perturbations. We computed aPT, iPT, and bPT to compare performance of the PCLCS with current management.

**Results:** Under current management, the median aPT, iPT, and bPT achieved in the 35 RSE patients were 2% (IQR [0, 21]%), 8% (IQR [0, 29]%), and 82% (IQR [37, 100]%). Under automated control the median aPT, iPT, and bPT in simulated patients were 0% (IQR [0, 0]%), 92.3% (IQR [90.2, 94.4]%), and 7.7% (IQR [5.6, 9.8]%). The average aPT, iPT, and bPT achieved by the PCLCS in rodents were 0%, 98.6% and 1.4%.

**Conclusions:** Under current management, burst suppression usually falls outside the clinically targeted range. Automated closed-loop control achieves significantly better performance in computer simulations and animal studies. Closed-loop control of burst suppression is a promising paradigm for enabling well-controlled clinical studies and ultimately for optimizing the safety of delivering pharmacologically induced coma.

**P60 – BEST POSTER**

Efficacy and safety of perampanel oral loading in post-anoxic super-refractory status epilepticus. A case series

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**Background:** Super-refractory non convulsive status epilepticus (NCSE) occurs in approximately 20-25% of patients with post-anoxic encephalopathy, following successful resuscitation after cardiac arrest. In selected patients with favorable multimodal prognostic indicators, aggressive treatment of super-refractory NCSE may lead to awakening and good neurological outcome.

**Methods:** We analyzed acute EEG changes, neurological outcome and adverse effects in consecutive post-anoxic patients with super-refractory NCSE treated with add-on oral loading of perampanel in the Cardiac Intensive Care Unit (ICU), Monza, Italy between 10/2015 and 10/2016 by retrospective chart review. Efficacy was defined when
Perampanel was the last antiepileptic drug introduced into the antiepileptic therapy within 72 h before the cessation of NCSE and without changes in the comedication. Clinical outcome was assessed using the cerebral performance category (CPC) at 3 months after ICU discharge.

**Results:** Eight post-anoxic patients with super-refractory NCSE were treated with perampanel (median initial dose 6 mg, range 6-12 mg) administered via nasogastric tube. Median age was 52 years (range 26–71). All patients had continuous EEG monitoring showing definite generalized NCSE with coma, diagnosed according to the Salzburg criteria. All patients had favorable multimodal prognostic indicators (presence of brainstem reflexes; presence of bilateral N20 responses; absence of periodic discharges/GPEDs). Perampanel was given after a median number of 3 antiepileptic drugs (range 2-5) and 3 anesthetic drugs (range 1-4), after a median time of 9.5 days (range 4-35). In 6 patients (75%), status epilepticus resolved within 72 hours after administration of Perampanel, without changing the comedication. Neurological outcomes at 3 months were return to normal or minimal disability in 4 patients (CPC 1-2, 50%), minimally conscious state in 1 patient (CPC 4, 12.5%) and death in 3 patients (CPC 5, 37.5%). No cardiorespiratory or cutaneous adverse effects was reported. A reversible cholestasis, which required no specific treatment, was observed in 5 patients (62.5%).

**Conclusions:** Perampanel 6-12 mg oral loading appeared an effective option in selected patients with post-anoxic super-refractory NCSE with good prognostic indicators. In this patient population, our safety data indicate a risk of reversible drug-induced cholestasis.

**P61**

**Newer antiepileptic agents in status epilepticus: evolution over ten years and correlation with prognosis**

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**Background:** Newer antiepileptic drugs (AEDs) are increasingly prescribed; however, relatively limited data are available concerning their utilization in status epilepticus (SE). Our aims were to explore the evolution in prescription patterns of newer and traditional AEDs in this clinical setting and their association with prognosis.

**Methods:** We analyzed our prospective adult SE registry over 10 years (2007-2016), and assessed the yearly use of newer and traditional AEDs and its association with mortality, return to baseline conditions at discharge, and SE refractoriness.

**Results:** Prescription of newer AEDs showed a marked increase, whereas traditional AEDs (if excluding benzodiazepines) declined over time. While outcome at discharge did not change notably during the study period, prescription of newer AEDs independently correlated to higher disability at discharge and higher rate of treatment failures, but not with mortality.

**Conclusion:** We observed a growing trend in newer AEDs prescription in SE over the last decade. However, our findings seem to suggest an associated increased risk of new disability and SE refractoriness. Pending prospective comparative studies, this may justify some caution in the routine use of newer AEDs in SE.

**P62**

**Topiramate in the treatment of generalized convulsive status epilepticus in adults: a systematic review with individual patient data analysis**

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**Background:** Individual patient data analyses have the potential to answer questions not posed by individual studies or conventional meta-analyses. In this systematic
review with individual patient data analysis we evaluated the role of topiramate (TPM) in generalized convulsive status epilepticus (GCSE), including super-refractory status epilepticus (SRSE).

**Methods:** MEDLINE, CENTRAL, ClinicalTrials.gov, LILACS, Google Scholar, and Opengrey.eu were systematically searched. Individual patient data were collected and analyzed. We compared patients who received TPM as last drug, which was followed by cessation of SE, to patient who received TPM but without termination of SE. We analyzed the following variables: age, gender, previous history of seizures, etiology, number of AEDs prior to TPM, maximum daily dose of TPM, patients with SE controlled, number of deaths, patients with TPM used as last AED.

**Results:** The literature search yielded 1,164 results. Individual patient data were available for 35 patients (6 with SRSE) from 5 studies. Among the 35 patients receiving TPM either as last drugs (n=20) or not (n=15), SE was controlled in 69%. Conversely, SE was terminated in 14/20 patients receiving TPM as last drug (70%). Only 6 patients (17%) received TPM for SRSE; in 5 of these cases, TPM was administered as last drug with resolution of SE in 4 cases. In 69% of cases TPM was used as third-line AED. There was no significant statistical significance between patients who received TPM as last drug and those who did not. Similarly, no difference was found comparing patients receiving TPM as last drug and achieving SE control with those receiving TPM as last drug but without termination of SE.

**Conclusions:** The lack of statistically significant difference is likely due to small sample size and statistical error type II. Evidence supporting the use of TPM in SRSE is insufficient. There is an unmet need for high-quality observational and interventional studies to evaluate the role of TPM in GCSE, including SRSE.

**P63  – BEST POSTER**

**Parenteral phenobarbital in status epilepticus revisited – Mayo Clinic experience**

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**Background:** The treatment of refractory status epilepticus (SE) with anesthetic medication dosages has been associated with poor outcome. The phenobarbital (PB) dosage used in the VA Cooperative trial and recommended in the 2016 AES Convulsive SE Guideline is 15 mg/kg. However, PB has fallen out of favor compared to non-sedating medications due to potential for respiratory suppression and prolonged sedation. We performed a retrospective review of use of PB at dosages below those prompting need for ventilatory support in the treatment of SE.

**Methods:** Forty patients were identified as having received PB in the neurologic intensive care unit at Mayo Clinic, Rochester, MN between 1 Jan 2011 and 31 Dec 2016 through our pharmacy dispensing database. Of these, eight received PB for SE who did not require ventilatory support (32 of these patients were excluded: received PB for maintenance therapy (15), PB administered to ventilated patient (14), treated for subtherapeutic levels (2), non-SE indication (1)). The EMR was reviewed to ascertain clinical data, prior treatments, therapeutic response, and outcome.

**Results:** Ages ranged from 24-77 years (median=64); all had focal SE, none were comatose. Seizure activity improved acutely following PB administration in seven, and stopped in six. Dosages ranged from 5-19.8 mg/kg (median=10 mg/kg); none required intubation and only one received supplemental oxygen. Patients received a median of four AEDs prior to PB; the median interval between first drug and PB was 23.5 hours. GCS did not change following PB administration. All but one had a decline of MAP >20 mmHg, but only one required intervention.

**Conclusions:** Moderate dose parenteral PB was effective in attaining seizure control in a significant proportion of non-comatose refractory SE patients. Ventilatory support
was not required for any patient and blood pressure support in only one. PB dosages below those in the 2016 AES Convulsive SE Guideline may be sufficient to stop SE. This dose strategy warrants further study.

P64

Increasing use of, but under-dosing with, levetiracetam in benzodiazepine refractory convulsive status epilepticus. Emergency clinicians need updated guidance on alternatives to phenytoin pending trial evidence

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Background: Newer alternatives to phenytoin, levetiracetam and valproate, for established convulsive status epilepticus (CSE) are attractive, though comparative efficacy and safety is not yet certain pending the outcome of a large trial now underway. We set out to establish the extent to which current practice in a UK regional neuroscience centre adhered to national/international guidance, and current evidence in this context.

Methods: From 133 episodes of SE identified prospectively by coding over 18 months, retrospective notes review identified 47 adults (≥16 years) with CSE. Patients with postanoxic SE, who arrived intubated, or with missing records were not included. Data on demographics, clinical SE features, treatment and outcomes were collected, and quality assured by the senior investigator. Adequate minimum dosing for each agent was defined ≥ 90% of the recommended mg/kg (levetiracetam 40; valproate 30; Phenytoin 20), with average UK adult weights used where this had not recorded.

Results: Benzodiazepines were the initial treatment in all patients. Of 34 patients treated with a 2nd line AED, 1 (3%) received Valproate, 18 (53%) levetiracetam and 15 (44%) phenytoin. Where the dose could be identified, this was most commonly 1000mg for levetiracetam and phenytoin, irrespective of weight. 82% of patients treated with levetiracetam had been under-dosed (mean dose 66% +/- SD29%), and 60% with Phenytoin (78 +/- 22%). 68% were admitted to ICU (mean stay 5 days), of whom 58% had received Levetiracetam and 42% phenytoin (not significant by drug or dose).

Conclusions: Levetiracetam is being increasingly used in CSE, despite not being licensed nor recommended in most guidance, and in advance of RCT evidence. Valproate is rarely used despite a comparable evidence base. Phenytoin, and especially levetiracetam are frequently under-dosed, despite a conservative threshold for levetiracetam (up to 60mg/kg is recommended by some). Under treatment is likely to affect patient outcomes, and may contribute to high ICU rates in this study. As alternatives to phenytoin are increasingly used, emergency clinicians need urgent guidance for appropriate dosing pending further evidence.

P65

Multicenter retrospective study of management of anesthetics drugs in convulsive status epilepticus in ICU

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Background: Convulsive Status epilepticus (CSE) is a common cause of admission in intensive care units (ICU), and patients frequently require mechanical ventilation, either for initiation of general anesthesia in case of refractory status epilepticus or for airway protection despite seizure cessation. Guidelines for the management of refractory status epilepticus recommend to maintain anesthetics drugs for 24h-48h, followed by gradual withdrawal. However there is currently no strong evidence to support this regimen. The cessation of anesthetics drugs at the time of ICU
admission seems to be a regular practice, but data regarding the management of general anesthesia in these patients are scarce.

Objectives: To evaluate the management of general anesthesia in patients admitted for SE in ICU, in particular the frequency and the safety of the cessation of anesthetics drugs at the time of ICU admission.

Methods: This is an ongoing multicenter retrospective observational study in five ICU. Inclusion criterion are: patient admitted in ICU for CSE and receiving mechanical ventilation between 01/01/2014 and 12/31/2016. Exclusion criteria are: age under 18 years, post anoxic state, traumatic brain injury. Data are collected retrospectively regarding past medical history of seizures, comorbidities, etiology, type and duration of status, reason for initial intubation (refractory SE or others), antiepileptic drugs (AED) administrated including benzodiazepines, continuous IV-AEDs and anesthetics drugs with the dosage and the duration, type and time of EEG monitoring. Data about outcomes are rescue of CSE, duration of mechanical ventilation, length of stay in ICU and mortality in ICU.

Status (results): Data are currently being collected, and medical files of patients are being reviewed.

Conclusions:
The aim of our study is to describe the current practice in the management of anesthetics drugs in patients admitted for convulsive status epilepticus under mechanical ventilation in ICUs.
The best management of anesthetics drugs regarding resolution of CSE and risk of life-threatening complications due to excessively aggressive treatment is not known. Our study may help design a prospective randomized study in the future, comparing pursuit of anesthetics drugs versus interruption upon arrival in ICU.

P66
A multicentre randomised controlled trial of levetiracetam versus phenytoin for convulsive status epilepticus in children (protocol): Convulsive Status Epilepticus Paediatric Trial (ConSEPT). A PREDICT study

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PREDICT21

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Background: Convulsive status epilepticus (CSE) is the most common life-threatening childhood neurological emergency. Despite this, there is a lack of high quality evidence supporting medication use after first line agents, with current treatment protocols based solely on non-experimental evidence and expert opinion. The current standard of care, phenytoin, is not ideal and associated with considerable adverse effects. A newer anti-convulsant, levetiracetam, can be given faster with a more tolerable side effect profile. The objective of the study is
to determine whether intravenous (IV) levetiracetam or IV phenytoin is the better second line treatment for the emergency management of CSE in children.

**Methods/Design:** 200 children aged between 3 months and 16 years presenting to 13 emergency departments in Australia and New Zealand with CSE, that has failed to stop with first line benzodiazepines, will be enrolled into this multicentre open randomised controlled trial. Participants will be randomised to 40mg/kg IV levetiracetam infusion over 5 minutes or 20mg/kg IV phenytoin infusion over 20 minutes. The primary outcome for the study is clinical cessation of seizure activity five minutes following the completion of the infusion. The primary outcome assessment will be video recorded and assessed by a primary outcome assessment team blinded to treatment allocation. Secondary outcomes include: Clinical cessation of seizure activity at two hours; Time to clinical seizure cessation; Need for rapid sequence induction; Intensive care unit (ICU) admission; Serious adverse events; Length of Hospital/ICU stay; Seizure status/death at one-month post discharge.

**Discussion:** We present the background, rationale, and design for a randomised controlled trial comparing levetiracetam to phenytoin in children presenting with CSE in whom benzodiazepines have failed. This study will provide high quality evidence for management of paediatric CSE post first-line benzodiazepines.

**Trial registration:** Prospectively registered with the Australian and New Zealand Clinical Trial Registry (ANZCTR):ACTRN12615000129583 (11/2/2015). UTN U1111-1144-5272.

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**P67 Brivaracetam in established status epilepticus – the Salzburg experience**


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**Background:** Brivaracetam (BRV) is a novel high affinity synaptic vesicle glycoprotein 2A (SV2A) ligand that is structurally related to Levetiracetam (LEV). Compared to its parent substance, its affinity to the ligand is more than 10-30% higher. Due to its lipophilic characteristics, it might have a stronger anticonvulsant effect and a quicker penetration across the blood brain barrier.

**Methods:** We analyzed treatment response, seizure outcome and adverse effect rates in add-on treatment with BRV in patients with established Status epilepticus (eSE) in 2016 at our department by retrospective chart view.

**Results:** BRV was administered intravenously in four patients (3 women) with eSE between 01/01/2016 and 12/31/2016. Median age was 53.5 (range 30-79) years. NCSE with and without coma was observed in two patients each. NCSE arose de novo, or was remote symptomatic in 2 patients each. The most frequent etiology was vascular in two patients. BRV was administered after a median number of 4 antiepileptic drugs (AEDs), range 3-9. The time of treatment initiation ranged from 10.5 hours to 12 days (median 4 days, in 75% of patients >72h). Immediate EEG or clinical improvement was observed in 2 patients. Median loading dose was 100 mg, intravenously over 15 minutes (range 50-200 mg), up titrated to a median daily dose of 100 mg/d (range 100 mg/d – 200 mg/d). Glasgow outcome scale (GOS) was 3 in median (range 3-5) with an improvement in all patients (100%) compared to admission. We observed no adverse effects (AEs) regarding cardio-respiratory function.

**Conclusion:** BRV might have a potential as novel AED in eSE as suggested by this preliminary case study. Its
promising potential might be caused by its ability to cross
the blood barrier faster than LEV and good safety profile.
Prospective studies for the use of BRV in eSE are required.

P68

**Population pharmacokinetic analysis of oxcarbazepine in patients with epilepsy**

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**Background:** Oxcarbazepine is a widely used anticonvulsant drug to treat focal seizure as monotherapy or adjunctive therapy. The mono-hydroxylated derivative (MHD) is the main metabolite which is responsible for most of the anticonvulsant activity. The objectives of this study are to develop a pharmacokinetic model of oxcarbazepine and to analyse the relationship between trough concentrations of the drug and occurrence of adverse event (AE) or seizure.

**Methods:** To develop a pharmacokinetic model of oxcarbazepine, the data from two studies were used; the data of 447 patients who had been enrolled in from Epilepsy Registry Cohort of Seoul National University Hospital since Feb 2011 and the data of pharmacokinetic study involving 40 patients evaluating oral loading of oxcarbazepine. Plasma concentrations of MHD were analysed using nonlinear mixed-effect modelling in NONMEM (ver 7.3). The first-order conditional estimation with interaction method was used to fit the plasma concentration-time data. Trough concentrations of each patient were calculated using the final pharmacokinetic model. The relation between trough concentrations and occurrence of AE or seizure were analysed using Students’ t-test.

**Results:** A one-compartment model with first-order absorption, and a proportional error model describes oxcarbazepine pharmacokinetics adequately. The body weight was significant covariate for the clearance and the volume of distribution of the drug and the use of concomitant drugs including carbamazepine, phenytoin, and phenobarbital which are known to be enzyme-inducers increased the clearance 1.38-fold. The trough concentrations of the drug were slightly higher in the patients group with AEs (mean ± SD; 13.4 ± 7.8 ng/mL) or with seizure episodes more than once (13.9 ± 7.6 ng/mL) compared to the non-AE group (12.4 ± 6.8 ng/mL) or non-seizure group (12.7 ± 7.2 ng/mL) but the differences were not statistically significant.

**Conclusions:** The population pharmacokinetic model developed in this study adequately described oxcarbazepine pharmacokinetics in patients with epilepsy. The covariates selected in this study including body weight and the use of concomitant drug are expected to be used to choose appropriate dosage regimen in the patients.

P69

**Time is brain in status epilepticus**

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**Background:** Status epilepticus (SE) is a neurologic emergency with a high morbi-mortality. It usually constitutes a diagnostic and therapeutic challenge for the physicians as the outcome is time-dependent.

**Methods:** Retrospective review of patients with SE, identified between 1/1/2014-12/15/2016 in two tertiary medical centers. The primary outcome was to analyze the prognosis and the role of timing in SE outcome.

**Results:** 108 patients (59% male). Median age 69.5; 43% had history of epilepsy. The most frequent clinical presentation was non-convulsive SE (NCSE) 57.4%. About etiology, 43.5% were considered acute symptomatic (15.7% stroke), 27.8% remote symptomatic (21.3% stroke or traumatic brain injury), 8.3% progressive symptomatic, 5.6% defined electroclinical syndrome and 14.8%
cryptogenic. 38 cases (35.2%) debuted in hospitalized patients. Regarding treatment, most of the patients (88%) weren’t controlled with first line, 64.8% had refractory SE. Main time variables analyzed were (median, hours): debut-hospital arrival (2.35), debut-neurology assessment (3.0), debut-first line treatment (3.0), debut-second line treatment (3.7), debut-third line treatment (7.25), debut-induced coma (35.0), debut-EEG (12.5) and duration of SE (25.5). A shorter time to start the first and second line treatment was associated with a shorter duration of SE. Poor functional status was seen in 32%, 19% died. Predicators of poor prognosis (PPP) in the global sample included life-threatening etiology (p=0.001), arising de novo in hospitalized patients (HP) (p=0.039), mSTESS (p<0.001) and duration of SE >24hours (p=0.02). Considering the different subgroups, the PPP in the NCSE focal without impairment of consciousness and aphasic SE were life-threatening etiology (p<0.001), mSTESS (p<0.001) and duration of SE >40hours (p<0.001); in NCSE focal with impaired consciousness, duration >24hours (p=0.04) and in the prominent motor symptoms SE were the presence of LPD (p<0.001), life-threatening etiology (p=0.019), HP (p=0.010) and mSTESS (p=0.023). NCSE was the subtype of SE more benefited by an early neurology assessment.

Conclusions: Duration of SE influences the prognosis of both the global sample and the NCSE subtypes. An earliest treatment is associated with reduced risk of intra-hospital mortality and poor functional status.

P70 – BEST POSTER

Perampanel in patients with refractory and super-refractory status epilepticus in a neurological intensive care unit - an update


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Purpose: In refractory status epilepticus (SE), GABAergic drugs become less effective and glutamate plays a major role in seizure perpetuation. Perampanel (PER) is the first orally active noncompetitive AMPA receptor antagonist for adjunctive treatment of refractory focal epilepsy.

Methods: We retrospectively analyzed treatment response, outcome, and adverse effects of add-on treatment with PER via nasogastric tube in patients with refractory SE in the Neurological Intensive Care Unit (NICU), Salzburg, Austria between 09/2012 and 12/2016.

Results: Twenty patients with refractory SE (80% women, median 70 years, 21 to 91) were treated with add on PER between 09/2012 and 12/2016. In four patients an intensified dosage approach was used. The most frequent SE type was nonconvulsive SE (NCSE) with (6/20, 30%) and without coma (11/20, 55%). PER was given after median 1.5 days [0.5 - 18.3] and four antiepileptic drugs [2-7]. In one patient (female, age 60 years), clinical improvement was observed within 24 h and EEG improvement within 60 h after administration of PER 12mg, while in another patient (female, age 66 years), clinical and EEG improvement was observed more than 48 h after administration of PER 6 mg. Median initial dose in the “standard” dose group was 4 mg [2–12, dose increase 2 to 4 mg per day]. Higher initial doses [median 32 mg; 20 - 32 mg] were used in the “intensified dosage” group. In one patient (female, age 21 years) with focal motor SE, clinical and EEG improvement was observed within 24 hours after PER 20 mg. Continuous cardiorespiratory monitoring showed no changes in both groups. In four patients with concomitant phenytoin, mild increase of liver enzymes was observed without clinical symptoms or abnormalities in liver sonography.

Conclusion: Though glutamate plays a major role in seizure perpetuation, PER could only ameliorate seizure activity in few patients with refractory SE. Long duration of SE before administration of PER, the route of administration, as well as relatively low doses in the majority of patients (16/20, 80%), might be responsible for the modest result. No cardiorespiratory adverse events or clinically relevant laboratory changes were observed associated with both “standard” and “intensified dose” PER administration.
P71

The impact of first response to out-of-hospital status epilepticus

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Background: In patients with status epilepticus (SE), prehospital response by emergency medical services (EMS) seems crucial for favourable course and outcome, but studies in this context are scarce. We sought to determine the impact of EMS response to out-of-hospital SE on outcome.

Methods: From 2005-2014, clinical EMS and in-hospital data were assessed in consecutive adult patients admitted to an academic medical center with out-of-hospital SE.

Results: Among 213 SE patients, 150 were admitted via the EMS. SE was confirmed within a mean of 199 minutes after admission and missed by the EMS in 55%, foremost in patients with increased age (p<0.001), a higher median Glasgow Coma Score (GCS) (p=0.013), without seizure history (p<0.001), and with acute/fatal etiologies (p=0.002). Patients with missed epileptic events were less likely to receive benzodiazepines before admission (p=0.001). Multivariable analysis uncovered that patients with missed epileptic events had increased odds for no return to functional baseline in survivors until discharge (OR=2.9; 95%CI 1.2-7.2; p=0.020) independent of age, acute/fatal etiology, GCS, Charlson Comorbidity Index, and SE duration. According to the multivariable model, missed epileptic event was more likely with older age, higher GCS and no seizure history. The area under the receiver operating characteristic curve for prediction of missed epileptic event by these variables was 0.818.

Conclusions: Out-of-hospital SE is missed especially in patients with increasing age, high initial GCS, and no seizure history. This calls for heightened awareness for SE in such patients, as missed epileptic events are associated with inappropriate treatment and increased odds for no return to functional baseline in survivors independent of established outcome predictors.

P72 – BEST POSTER

Phase I study to determine the pharmacokinetics, pharmacodynamics, and safety of IV ganaxolone in healthy adults

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Background: Ganaxolone (GNX), a synthetic analog endogenous allopregnanolone, is in development for treatment of epilepsy and other neurological and psychiatric conditions. GNX allosterically modulates γ-aminobutyric acid type A (GABAA) receptors and has sedative, anxiolytic and anticonvulsant effects. GNX IV is being developed to expand treatment options for patients with status epilepticus. The objective of this study was to evaluate the safety, pharmacokinetics (PK), and pharmacodynamics (PD) of GNX IV administered as a bolus dose and continuous infusion to healthy participants.

Methods: This was a single site, sequential cohort evaluation of GNX IV. The study consisted of 6 cohorts. PK, changes in EEG, BIS, and sedation scores, and safety (ECG, vital signs, physical examination findings, and adverse events) were assessed following a single bolus and bolus dosing followed by continuous infusion of GNX IV. The PK from each cohort was modeled to select the doses for subsequent cohorts. One cohort had an objective to explore the sedative effects of ganaxolone, including the potential of the drug to induce burst suppression

Results: Thirty-six subjects received study drug and 35 subjects completed the initial 5 cohorts. Treatment emergent adverse events were mild in severity and
resolved without intervention. There were no clinically significant changes in physical exams, vital signs, ECGs, and laboratory values. Changes in BIS and sedation scores were evident within 5-15 minutes of infusion start and the majority returned to baseline within 30 minutes post bolus dose. GNX concentrations in plasma were generally proportional to the administered dose. Potential anticonvulsant plasma concentrations were achievable with a bolus dose. After the IV bolus dose or cessation of the IV infusion dose, concentrations of GNX in plasma declined in a multi-phasic manner.

Conclusions: GNX administered as a rapid IV bolus or bolus with continuous infusion was generally safe and well tolerated; there were no safety issues that limit getting to a potentially efficacious plasma concentration in a short period of time. BIS and qualitative EEG changes correlated with expected GABAA mechanism of action. Predictable PK from this study enables dosing guidance for GNX IV.

P73

Status epilepticus as a manifestation of paradoxical aggravation by treatment with newer-generation antiepileptic drugs

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Background: Seizure aggravation by antiepileptic drugs (AEDs) is defined as a paradoxical reaction when an AED increases the frequency and/or severity, and/or changes the pattern of a seizure type against it is usually effective, or when it leads to the onset of new types of seizures, or the occurrence of status epilepticus (SE). The purpose of our study is to report cases with SE caused by treatment with some of the newer-generation AEDs.

Methods: The study was performed with the participation of 1259 consecutive patients with epilepsy who attended the Clinic of Neurology at the University Hospital in Plovdiv, Bulgaria for a regular examination or in cases of unsatisfactory seizure control or adverse events from treatment. In 324 patients the antiepileptic treatment included some of the newer-generation AEDs. The data about epilepsy, antiepileptic treatment and its effect on seizure frequency and severity were collected through an interview, examination of the patients’ medical documentation and a prospective study of all participants for at least 6 months from the initiation of a newer-generation AED.

Results: SE as a manifestation of paradoxical aggravation by newer-generation AEDs was reported in 5 (1.54%) patients with refractory epilepsy (4 women, mean age of 34 years). In a male participant with focal epilepsy convulsive SE was reported 11 days after an increased dose of oxcarbazepine (1800 mg/d) and topiramate (200 mg/d). In 2 patients with focal/generalized epilepsy the treatment with levetiracetam 3000/2000 mg/d induced seizure aggravation and convulsive SE in the following 1-5 months. In 1 patient with focal epilepsy the treatment with pregabalin 225 mg/d induced focal convulsive SE in 1 week. In 1 patient with focal epilepsy the dose increase of lacosamide from 200 to 300 mg/d caused seizure aggravation and convulsive SE in 1 month. In all cases adaptation of therapy resulted in seizure improvement.

Conclusions: Despite the low frequency of SE as a manifestation of seizure aggravation, newer-generation AEDs may have also the potential of causing it. This necessitates timely focusing of attention on effects from treatment with the purpose of prevention of serious complications.

P74 – BEST POSTER

Characterization of allopregnanolone pharmacokinetics in dogs with naturally-occurring epilepsy to support use in the initial treatment of status epilepticus

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**Background:** Allopregnanolone is a naturally-occurring neurosteroid that is a positive allosteric modulator of synaptic and extrasynaptic GABA _A_ receptors. A Phase III clinical trial is evaluating allopregnanolone administered by continuous intravenous (IV) infusion as a treatment for super-refractory status epilepticus (SE) in patients under general anesthesia in an intensive care setting. We hypothesize that allopregnanolone possesses the requisite pharmacokinetic (PK) and pharmacodynamic properties to support its use as an initial IV bolus treatment for SE. One approach to testing this hypothesis is the use of dogs with naturally-occurring epilepsy, which is similar to human epilepsy in electroencephalographic presentation and response to therapy. Previously, our group has shown that fosphenytoin and levetiracetam exhibit comparable efficacy in SE in dogs and humans. Our study objectives were to assess the tolerability and develop a PK model of allopregnanolone following a 5 minute IV infusion, a clinically applicable regimen for the initial treatment of SE.

**Methods:** Four dogs with naturally-occurring epilepsy were used, with two on phenobarbital. A 1 mg/kg allopregnanolone dose (1.5 mg/mL in 24% sulfobutyl ether β-cyclodextrin) was infused over 5 minutes. Blood samples were collected between 0 to 8 hours following dosing. Animals were observed for ataxia, vomiting, diarrhea, and lethargy prior to and for 60 minutes after the infusion, and thereafter at each subsequent sampling time. Plasma concentrations were measured using a UPLC-MS/MS system. Non-compartmental and compartmental modeling were performed.

**Results:** The only adverse effects observed were two dogs on phenobarbital who exhibited ataxia and somnolence 3 minutes after start of infusion, and recovered within 10 minutes. Plasma concentrations at 2 minutes post-infusion were ~5000 ng/mL, declining to 130-700 ng/mL at 30 minutes. Concentration-time profiles were best fit by a two-compartment model. Phenobarbital was associated with a greater clearance and shorter elimination half-life.

**Conclusions:** A 1 mg/kg allopregnanolone dose infused over 5 minutes appears safe and results in attainment of plasma concentrations greater than those associated with seizure cessation in rodents. At this dose, transitory sedation may occur in dogs receiving phenobarbital. Our results support further evaluation of allopregnanolone for efficacy in the initial SE treatment in dogs and humans.

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**P75 – BEST POSTER**

**Side effects of antiepileptic drugs in anti-LGI1 encephalitis**

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**Background:** Anti-leucine rich glioma inactivated 1 (LGI1) encephalitis is a rare autoimmune condition presenting mainly with altered mentality, cognitive dysfunction and seizure. Antiepileptic drugs (AEDs) are usually initiated to control faciobrachial dystonic seizure and other seizure manifestations, but the clinicians often change AEDs during the treatment course and drug side effects are among the main cause. We investigated type and frequency of side effects of AEDs in patients with anti-LGI1 encephalitis.

**Methods:** We screened the patients who diagnosed with anti-LGI1 encephalitis and treated with AEDs for seizure control in three hospitals from October 2012 to September 2016. Medical records were reviewed to identify the AEDs and their side effects in these patients.

**Results:** Among the 20 patients who were treated with AEDs, 10 (50%) changed their AEDs due to adverse cutaneous drug reaction (ACDR). Eight of them presented with maculopapular eruption, one with drug rash with eosinophilia and systemic symptoms syndrome, and one with eczema. AEDs that were discontinued in association with ACDR include oxcarbazepine (7 patients), lamotrigine (2 patients), phenytoin (2 patients), carbamazepine (1 patient), and valproate (1 patient).
patient), and levetiracetam (1 patient). Oxcarbazepines were discontinued in two additional patients due to hyponatremia. Six patients (30%) discontinue or reduce the dose of levetiracetam for psychiatric manifestations including irritability/aggressive behavior (4 patients) and depressive mood (2 patients).

**Conclusions:** ACDR was highly frequent side effect leading to the discontinuation of AEDs in patients with anti-LGI1 encephalitis and causative drugs were mostly consist of aromatic AEDs. Clinicians should consider ACDR, psychiatric side effects, and hyponatremia when selecting AED for the treatment of anti-LGI1 encephalitis.

**P76  – BEST POSTER**

**Patterns of emergency treatment with benzodiazepine in routine practice in patients with refractory status epilepticus prior to their enrollment in a clinical trial**

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**Background:** Early adequate dosing of benzodiazepines is recognized as key to early seizure termination. Prior research from a small number of sites, however, suggests that emergency treatment of patients with status epilepticus (SE) often differs from that indicated in published guidelines. As part of ongoing assessments of clinical care prior to enrollment of patients with benzodiazepine refractory SE in a clinical trial, we describe patterns of lorazepam, diazepam, and midazolam dosing in the prehospital and emergency department (ED) setting.

**Methods:** Descriptive evaluation of treatments given prior to enrollment in ESETT, an ongoing clinical trial of second-line anticonvulsants in SE refractory to benzodiazepine treatment. Enrollment criteria include persistent seizures despite adequate doses of benzodiazepine. The number, dose, and timing of benzodiazepine administrations, as well as agent and cumulative dose per patient given prior to enrollment are evaluated. Cumulative doses included all agents and were considered in lorazepam equivalents (10 mg midazolam or diazepam = 4 mg lorazepam equivalents). Enrollment occurred at the moment of administration of a second-line study drug.

**Results:** In 207 subjects enrolled at 43 sites at the time of this analysis, there were 511 benzodiazepine administrations (312 lorazepam, 159 midazolam, 40 diazepam). Most diazepam administrations were prior to emergency medical services (EMS) arrival (66%), most midazolam administrations were by EMS (82%), and most lorazepam administrations were in the ED (86%). Among 139 adults and children >32 kg, 47% had a cumulative dose of 4-5 mg lorazepam equivalents, 23% had 6-7 mg, 14% had 8-9 mg. The dose per administration of lorazepam was 2 mg in 79%, and was 4 mg in 13%; 50% of midazolam administrations were <=4 mg, and 9% were 10 mg; diazepam was usually given as 5 mg or 10 mg administrations. Underdosing was similar in prehospital and ED settings.

**Conclusions:** Underdosing of benzodiazepines as compared to recommendations in published guidelines and in FDA labelling is common in this geographically diverse US set of patients. The low doses used per administration, in both ED and prehospital settings, suggest this represents practice culture rather than an artifact in practice driven by enrollment in the study.

**P77  – BEST POSTER**

**PK-PD studies of intramuscular allopregnanalone in a mouse model of pharmacoresistant status epilepticus**

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**Background:** Status epilepticus (SE) treatment requires
administration of fast acting antiseizure agents, which are generally delivered by the intravenous (IV) route. Intramuscular (IM) injection provides an opportunity for more rapid dosing in the field by emergency personnel and lay caregivers. Allopregnanolone (3α-hydroxy-5α-pregn-20-one; 5α,3α-P), an endogenous neurosteroid, is a positive allosteric modulator of synaptic and extrasynaptic GABA_A receptors currently under evaluation as a treatment for super-refractory SE. 5α,3α-P exerts anticonvulsant activity in various animal seizure models, including models of SE. The objective of this study was to demonstrate the activity of 5α,3α-P in the treatment of SE induced by the chemical threat agent tetramethylenedisulfotetramine (TETS) and to determine the blood and brain levels associated with seizure termination. 5α,3α-P was administered at a delayed time after SE onset when mice are refractory to standard-of-care treatment.

Methods: Solutions of 5α,3α-P were made in 6% (1.5 mg/ml) and in 24% (6-12 mg/ml) sulfobutylether-β-cyclodextrin sodium salt (Captisol®) in 0.9% saline. SE was induced in mice with TETS (0.2 mg/kg IP) followed by riluzole (10 mg/kg IP), which prevents rapid lethality and permits persistent SE. 5α,3α-P or vehicle was delivered IM 40 min after the first myoclonic body twitch. Mice were observed for 1 h to assess seizure termination and scored for lethality up to 72 h after dosing. 5α,3α-P plasma and brain levels were determined by LC-MS.

Results: 5α,3α-P at doses of 1.5, 3, 6 and 12 mg/kg terminated SE and prevented mortality in 70%, 77%, 80% and 91% of animals, respectively. The corresponding Cmax values were 267, 645, 1026 and 1628 ng/ml. The mean terminal elimination half-life was 50 min.

Conclusions: Our results demonstrate that IM 5α,3α-P rapidly terminates persistent behavioral and electrographic SE and improves long term survival in a dose-dependent fashion. Parenteral 5α,3α-P may be useful for the acute treatment of SE. This work was supported by the NINDS CounterACT Program (grant U54 NS079202).
The 7th London-Innsbruck Colloquium on Status Epilepticus and Acute Seizures

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Stephan Mayer (Detroit, USA)  
Eric Rosenthal (Boston, USA)  
Matthew Walker (London, UK)
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Thursday, 6 April 2017
19:30 – 24:00

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Patients 2 years of age or older who present with SRSE are eligible for enrollment and potential randomization in the trial if they:

• have failed 1st and 2nd line anti-epileptic drugs (AEDs), and
• are candidates to begin 3rd line agents or have already failed one or more wean attempts from 3rd line agents

SRSE is a potentially life-threatening form of Status Epilepticus (SE) that continues or recurs for >24 hours despite multiple therapeutic interventions (first-, second-, and third-line anesthetic agents). There are currently no FDA-approved treatments for SRSE.

For additional information or to refer a potential patient for the STATUS Trial, please visit www.statustrial.com