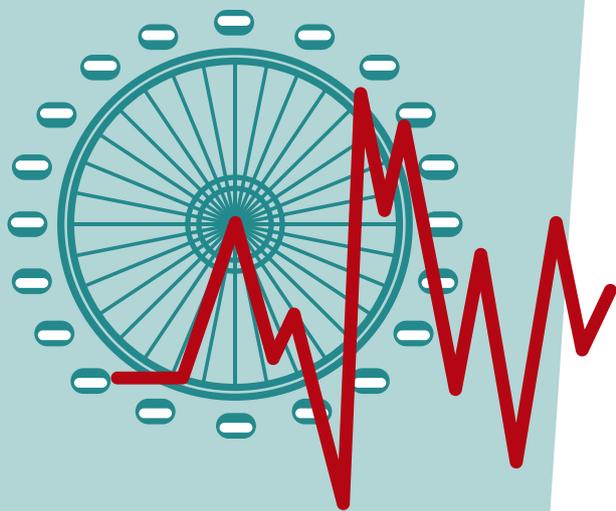


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**THE
7TH LONDON-INNSBRUCK
COLLOQUIUM
ON STATUS EPILEPTICUS
AND ACUTE SEIZURES**

7-9 APRIL 2019

**THE FRANCIS CRICK INSTITUTE
LONDON, UK**

**HELD UNDER THE AUSPICES OF
THE ILAE BRITISH CHAPTER**

**FINAL
PROGRAMME**

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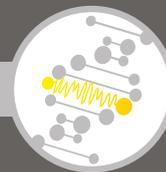


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Reference: 1. Pal DK, Pong AW, Chung WK. *Nat Rev Neurol* 2010; 6:445–53.

EU/CLN2/0645 March 2019

PATRONS

ILAE British Branch
53 Dundee Road
London, SE25 4QN
United Kingdom

University College London
Institute of Neurology
Queen Square
London WC1N 3BG
United Kingdom

Paracelsus Medical University
Christian Doppler Klinik
Ignaz Harrer Straße 79
5020 Salzburg
Austria

CHAIRS

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



**CONFERENCE
VENUE**

The Francis Crick Institute
1 Midland Road
London NW1 1ST



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DEAR FRIENDS AND COLLEAGUES,

We offer you a warm welcome to the 7th London-Innsbruck Colloquium on Status Epilepticus and Acute Seizures.

The colloquia have been held biannually since 2007 (London 2007, Innsbruck 2009, Oxford 2011, Salzburg 2013, London 2015, Salzburg 2017) and have become a popular feature of the epilepsy calendar. Over this period exciting advances have been made in the field, with better mechanistic understanding of new treatments and novel clinical strategies. Some of these were first discussed at previous colloquia, and this meeting too is similarly focused on cutting edge research and clinical practice.

We hope you will enjoy the programme which this year has several new features, including a pre-colloquium teaching course, a Nobel Laureate Lecture, parallel workshops and two data blitz sessions. The underpinning principles of the meeting though have not changed. As has been the case in all previous colloquia, we want to encourage and nurture intensive discussion. We have deliberately left space in the programme for the audience to question and challenge the speakers – and please feel free to do so. It is our belief, as a fundamental pillar of the colloquia, that academic debate is at the heart of all learning and discovery, and we hope you will all join in this endeavour.

The venue chosen this time is the Francis Crick Institute - a biomedical discovery institute devoted to understanding the fundamental biology of disease - and this is a perfect setting for achieving the colloquium aims, not least as it is housed in a spectacular building custom-built to stimulate scientific medicine.

Although the programme has increased in size, we still have worked to retain the collegiate and friendly character that has marked out the previous meetings, and

to provide opportunities for meeting and interacting with new and old colleagues. The conference dinner is to be held in the splendid Athenaeum Club and a Young Epilepsy Society meeting in a (less salubrious) pool club, and both should be a lot of fun.

Finally, some acknowledgements are in order. First, we would like to thank our conference organizing team, led by Mrs Ina Kähler, from PCO Tyrol Congress, and also Juliet Solomon and Hannah Stapley from the ILAE British Branch, for for their tremendous work. Also, the academic activities of this conference would not have been possible without the generous support of our sponsors listed on page 87 of this booklet, and we offer our sincere thanks to them all. We are grateful too for the patronage of this conference by University College London, Paracelsus Medical University Salzburg, the ILAE-British Branch and ILAE-Europe.

The colloquium prides itself on having much on offer to enjoy. And so it is our sincere pleasure to welcome you back to London, and to the Francis Crick Institute, for what we hope will be an entertaining, instructive and enjoyable three days.

With very best regards



Eugen Trinkka



Simon Shorvon



Matthew Walker

Simon Shorvon, Eugen Trinkka and Matthew Walker
(Co-organisers)

INFORMATION FOR SPEAKERS

Please make sure to bring your **PowerPoint presentation on a USB-stick to the speaker ready room** at the Crick Institute 2 hours prior to the start of your session.

Do not bring your own laptop for the presentation. In case your presentation contains video sequences, please ensure to pack them with a standard codec and do not store them in a Quick Time format since this may not be compatible with PowerPoint presentations.

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

Disclosure of potential conflicts of interest

Speakers at the 7th 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. Poster measures must not exceed A1 format (59,4 cm / 23,4" in width and 84,1 cm / 33,1" in height). No other formats are allowed! Posters exceeding the above-mentioned directions cannot be displayed. Mounting material will be provided on site.

All posters should be displayed during the entire Colloquium and mounted on Sunday, April 7th in the morning. They must be taken down on Tuesday, April 9 by the end of the colloquium. All posters not taken down by then will be discarded. If you do not remember your poster board number, please look it up in the list of posters.

Poster discussion:

There are time slots explicitly dedicated to the posters every day. The dates and times are scheduled as follows:

Sunday, April 7: 12:40 – 14:00

Monday, April 8: 11:50 - 13:00

Tuesday, April 9: 12:00 – 13:00

During these times, you or one of your co-authors should be at your poster site and be prepared to answer questions



Connecting with **patients**

" My journey with epilepsy started out rocky, but evolved into one of self-discovery. It's allowed me to look at my life with a new pair of eyes, change my behavior, and finally think outside the box."

LaKeisha, living with epilepsy

UCB has a passionate, long-term commitment to help patients and families living with severe diseases lead normal, everyday lives.

Our ambition is to offer them innovative new medicines and ground-breaking solutions in two main therapeutic areas: neurology and immunology. We foster cutting-edge scientific research that is guided by patients' needs.

Sándor Beniczky, Roskilde, Denmark
Ahmad Beydoun, Beirut, Lebanon
Nadir Bharucha, Mumbai, India
Meir Bialer, Jerusalem, Israel
Peter Blain, Newcastle upon Tyne, United Kingdom
Tom Bleck, Chicago, USA
Richard Chin, Edinburgh, United Kingdom
Hannah Cock, London, United Kingdom
Andrew Cole, Boston, USA
Mark Cook, Melbourne, Australia
Peter Crino, Baltimore, USA
Helen Cross, London, United Kingdom
Monica Ferlisi, Verona, Italy
Alon Friedman, Halifax, Canada
Renzo Guerrini, Florence, Italy
Cecil Hahn, Toronto, Canada
Raimund Helbok, Innsbruck, Austria
David Henshall, Dublin, Ireland
Sara Hocker, Rochester, USA
Reetta Kälviäinen, Kuopio, Finland
Peter Kaplan, Baltimore, USA
Jaideep Kapur, Charlottesville, USA
Christoph Kellinghaus, Osnabrück, Germany
Matthias Koepp, London, United Kingdom
Dimitri Kullmann, London, United Kingdom
Lieven Lagae, Leuven, Belgium
Stéphane Legriel, Le Chesnay, France
Markus Leitinger, Salzburg, Austria
Holger Lerche, Tübingen, Germany
Brian Litt, Philadelphia, USA
Tobias Loddenkemper, Boston, USA
Daniel Lowenstein, San Francisco, USA
Rosalyn Moran, London, United Kingdom
Ronit Pressler, London, United Kingdom
Ashalatha Radhakrishnan, Thiruvananthapuram, India
Shamima Rahman, London, United Kingdom
Michael Rogawski, Sacramento, USA
Eric Rosenthal, Weston, USA
James Rothman, London, United Kingdom
Stephan Rügg, Basel, Switzerland
Simon Shorvon, London, United Kingdom
Nicola Specchio, Rome, Italy
Eugen Trinkka, Salzburg, Austria
Annamaria Vezzani, Milan, Italy
Matthew Walker, London, United Kingdom
Claude Wasterlain, Los Angeles, USA
Rob Wykes, London, United Kingdom



SATURDAY, APRIL 6TH, 2019

09.30 - 17.00 Pre-colloquium Teaching Course on EEG in status epilepticus and on the intensive care unit

This course will be held at the Institute of Education, **20 Bedford Way, London**. It will be taught by an international faculty who are leaders in the field, and delegates will receive a pack of teaching materials.

The course is designed for trainees and consultant level clinicians and for technical staff. Details on the programme can be found on <https://ilaebritish.org.uk/events/eeg-in-status-epilepticus-and-on-the-intensive-care-unit/>

SUNDAY, APRIL 7TH, 2019

09.15 - 09.30 Introduction

Wellcome auditorium

Simon Shorvon, Eugen Trinko, Matthew Walker

09.30 - 12.40 Session 1: Networks and novel targets

Wellcome auditorium

Chairs: Annamaria Vezzani, Alon Friedman

09.30 - 10.10 Gene therapy for closed-loop seizure suppression

Dimitri Kullmann

10.10 - 10.40 Coffee break

10.40 - 11.20 Secondly generalized convulsive status epilepticus: circuits and mechanisms

Jaideep Kapur

11.20 - 12.00 Dynamic causal modeling of the EEG in epilepsy

Rosalyn Moran

12.00 - 12.40 Targeting reactive oxygen species in status epilepticus

Matthew Walker

10.40 - 12.40 Parallel session: Workshop - Outcomes in status epilepticus

Seminar suite

Chairs: Helen Cross, Holger Lerche

Outcome of childhood convulsive status epilepticus

Richard Chin

Electrographic seizure burden and outcome following paediatric status epilepticus

Cecil Hahn

Why do patients die after status epilepticus?

Sara Hocker

- 12.40 - 14.00 Lunch break & posters & conference photograph
- 14.00 - 16.00 Session 2: Biomarkers**
Seminar suite
Chairs: Peter Crino, Claude Wasterlain
- 14.00 - 14.40 MicroRNAs as biomarkers and treatment targets in status epilepticus
David Henshall
- 14.40 - 15.20 Biomarkers of inflammation and reactive oxygen species in status epilepticus; implications for therapy
Annamaria Vezzani
- 15.20 - 16.00 Blood-brain barrier disruption in status epilepticus: mechanisms and role in epileptogenesis
Alon Friedman
- 14.00 - 16.00 Parallel session: Workshop - When backs are against the wall. The clinical management of status epilepticus in specific situations**
Wellcome auditorium
Chairs: Reeta Kälviäinen, Lieven Lagae
- Management of status epilepticus in palliative care patients
Reeta Kälviäinen
- Status epilepticus in pregnancy - can we frame a uniform treatment protocol?
Ashalatha Radhakrishnan
- A ketamine clinical trial in status epilepticus
Eric Rosenthal
- 16.00 - 16.30 Coffee break
- 16.30 - 17.40 Session 3: Physical treatments of status epilepticus**
Wellcome auditorium
Chairs: Tom Bleck, Matthias Koepp
- 16.30 - 17.10 Hypothermia as a treatment of status epilepticus
Stéphane Legriel
- 17.10 - 17.40 Neurostimulation in the treatment of status epilepticus
Eugen Trinká
- 19.30 Colloquium Dinner**
at The Athenaeum Club, London

MONDAY, APRIL 8TH, 2019

- 08.30 - 10.00** **Session 4 : Hullabaloo-Controversies**
Wellcome auditorium
Chairs: Meir Bialer, Mark Cook
- 08.30 - 09.00 Lessons from the ESSET trial
Hannah Cock
- 09.00 - 09.30 Do neurosteroids have any future in the treatment of status epilepticus?
Mike Rogawski
- 09.30 - 10.00 What is the role of next generation sequencing in status epilepticus?
Renzo Guerrini
- 10.00 - 10.30 Coffee break
- 10.30 - 11.50** **Session 5: Big data, seizure detection and prediction**
Wellcome auditorium
Chairs: Daniel Lowenstein, Christoph Kellinghaus
- 10.30 - 11.10 New avenues in seizure detection and prediction
Mark Cook
- 11.10 - 11.50 Big data – future roles in status epilepticus
Brian Litt
- 11.50 - 13.00 Lunch & posters
- 13.00 - 14.00** **Satellite Symposium Zogenix**
Wellcome auditorium
Premature mortality in epileptic encephalopathies: Towards a better understanding?
- 13.00 - 13.05 Welcome and introduction
Matthew Walker
- 13.05 - 13.20 The value of preclinical models?
Benoit Martin
- 13.20 - 13.35 Neuropathology: Insights and challenges
Maria Thom
- 13.35 - 13.50 Clinical and family/patient perspectives
Richard Chin
- 13.50 - 14.00 Where might such understanding lead us?
Matthew Walker

- 14.00 - 15.30** **Session 6: Genes and paediatrics**
Wellcome auditorium
Chairs: Richard Chin, Renzo Guerrini
- 14.00 - 14.30 Status epilepticus and genetic variations in sodium channel genes
Holger Lerche
- 14.30 - 15.00 Status epilepticus and mTOR signaling
Peter Crino
- 15.00 - 15.30 The role of PCDH19 in refractory status epilepticus
Nicola Specchio
- 14.00 - 15.30** **Parallel session: Workshop - Novel variants of status epilepticus: de novo status and status due to nerve gas**
Seminar suite
Chair: Tom Bleck
- Prospective evaluation of new-onset seizures presenting as status epilepticus
Ahmad Beydoun
- Neurological consequences of organophosphate poisoning
Peter Blain
- Role of KCNQ2/3 potassium channels in cholinergic status epilepticus
Jaideep Kapur
- 15.30 - 16.00 Coffee break
- 16.00 - 16.30** **Session 7: Nobel laureate lecture**
Wellcome auditorium
Chairs: Simon Shorvon, Matthew Walker
- New insights into the mechanism of synchronous neurotransmitter disease
Professor James Rothman
- 16.30 - 18.30** **Session 8: Paediatrics and research networks**
Wellcome auditorium
Chairs: Cecil Hahn, Reetta Kälviäinen
- 16.30 - 17.00 The treatable causes of neonatal status epilepticus
Ronit Pressler
- 17.00 - 17.30 The SENSE registry of status epilepticus
Christoph Kellinghaus
- 17.30 - 18.00 The European Reference Network for rare and complex epilepsies epiCARE and its role in status epilepticus
Helen Cross

18.00 - 18.30 Update on North American pediatric convulsive status epilepticus research networks
Tobias Loddenkemper

16.30 - 18.30 Parallel session: Data blitz – epidemiology, outcome and novel clinical treatments

Seminar suite

Chairs: Sara Hocker, Monica Ferlisi

International panel: Rajashekhar Reddi, Sashendra Saxena

O-01 Epidemiology of status epilepticus in adults: data on two population based studies in Eastern Finland

Anne-Mari Kantanen, Joni Sairanen, Reetta Kälviäinen (Kuopio, Finland)

O-02 30-day re-admission after status epilepticus in Unites States: Insights from nationwide re-admission database

Monica B. Dhakar, David Thurman, Hiba A. Haider, Andres R. Rodriguez, Nathalie Jette, Edward Faught (Atlanta, New York; United States)

O-03 Status epilepticus mortality score after 30 days of hospital discharge: Development and validation using competing risks analysis

Somsak Tiamkao, Prapassara Sirikarn, Porjai Pattanittum (Khon Kaen, Thailand)

O-04 Cause of death in status epilepticus patients

Somsak Tiamkao, Prapassara Sirikarn, Porjai Pattanittum (Khon Kaen, Thailand)

O-05 Factors related to the development of mesial temporal sclerosis after status epilepticus

Estevo Santamarina, Silvana Sarria, Laura Abraira, Elena Fonseca, Xavier Salas - Puig, Manuel Quintana, Manuel Toledo (Barcelona, Spain)

O-06 Neurological outcome of post-anoxic refractory status epilepticus after aggressive treatment

Simone Beretta, Anna Coppo, Elisa Bianchi, Clara Zanchi, Davide Carone, Andrea Stabile, Giada Padovano, Endrit Sulmina, Graziella Bogliun, Giuseppe Foti, Carlo Ferrarese, Ettore Beghi, Leonello Avalli (Monza, Milano; Italy)

O-07 Prolonged seizures in children

Clodagh Mitchell, Libby Dickson, Paul Leonard, Celia Brand, Ailsa McLellan, Jay Shetty (Edinburgh, United Kingdom)

- O-08** Long-term safety and efficacy of add-on cannabidiol (CBD) treatment in patients with Lennox Gastaut Syndrome in an open-label extension trial (GWPCARE5)
Richard Chin, Anup Patel, Antonio Gil-Nagel, Wendy Mitchell, M Scott Perry, Arie Weinstock, Lauren Whyte, Kevan VanLandingham (Columbus, USA, Madrid, Spain, Los Angeles, USA, Fort Worth, USA, Buffalo, USA, Cambridge, UK, Carlsbad, USA)
- O-09** Serum neurofilament light chain as a prognostic marker in post-anoxic encephalopathy
Giulio Disanto, Chiara Prosperetti, Claudio Gobbi, Christian Barro, Zuzanna Michalak, Tiziano Cassina, Jens Kuhle, Gabriele Casso, Pamela Agazzi (Lugano, Basel, Ticino; Switzerland)
- O-10** Responsive neurostimulation therapy for super-refractory autoimmune epilepsy
Anteneh Feyissa, William Tatum, Jeffrey Britton (Jacksonville, Rochester; United States)
- O-11** Updated data on the tocilizumab treatment in new onset refractory status epilepticus
Hyoshin Son, Soon-Tae Lee, Hye-Rim Shin, Eun-Young Kim, Woo-Jin Lee, Kon Chu, Kyung-II Park, Sang Kun Lee (Seoul, South Korea)
- O-12** Combination therapy of immunoglobulin, Rituximab, and Tocilizumab in treating acute autoimmune encephalitis
Woo-jin Lee, Han-Sang Lee, Hye-Rin Shin, Eun-Young Kim, Hyoshin Son, Yong-Won Shin, Hyeyeon Chang, Soon-Tae Lee, Kyung-II Park, Kon Chu, Sang Kun Lee (Seoul, South Korea)

TUESDAY, APRIL 9TH, 2019

- 08.30 - 10.00** **Session 9: Sponsored talks, part I: Novel drugs and devices in development in status epilepticus and acute seizures**
Wellcome auditorium
Chairs: Daniel Lowenstein, Matthias Koepp
- 08.30 - 09.00 Management of prolonged seizures and myoclonic status in CLN2 disease: has this changed over time?
Nicola Specchio (on behalf of Biomarin Pharmaceuticals, Inc.)
- 09.00 - 09.30 Staccato Alprazolam for acute treatment of seizures
Jouko Isojarvi (on behalf of Engage Therapeutics, Inc.)
- 09.30 - 10.00 Brain distribution and SV2A receptor occupancy of Brivaracetam and Levetiracetam - Comparative PET studies in rodents, primates and healthy human subjects
Felix Rosenow (on behalf of UCB, S.A.)
- 10.00 - 10.30 Coffee break
- 10.30 - 12.00** **Session 9: Sponsored talks, part II: Novel drugs and devices in development in status epilepticus and acute seizures**
Wellcome auditorium
Chairs: Daniel Lowenstein, Peter Kaplan
- 10.30 - 11.00 Non-Convulsive status epilepticus: letting go of old traditions
Josef Parvizi (on behalf of Ceribell, Inc.)
- 11.00 - 11.30 Enabling drug delivery technologies to address unmet needs in epilepsy
Adrian Rabinowicz (on behalf of Neurelis, Inc.)
- 11.30 - 12.00 Vagus nerve stimulation in super refractory status epilepticus
Kristl Vonck (on behalf of LivaNova, Plc.)
- 12.00 - 13.00 Lunch & Posters
- 13.00 - 14.00** **Session 10: Novel treatment approaches in status epilepticus**
Wellcome auditorium
Chairs: Brian Litt, Nadir Bharucha
- 13.00 - 13.30 Lessons from the Sage trial
Andrew Cole
- 13.30 - 14.00 Polytherapy for status epilepticus: the proof of the pudding
Claude Wasterlain
- 14.00 - 14.30 Coffee break

- 14.30 - 16.30** **Session 11: Novel drugs in the treatment of status epilepticus**
Wellcome auditorium
Chairs: Nicola Specchio, Tobias Loddenkemper
- 14.30 - 15.00 New treatments of mitochondrial disease and their impact on status epilepticus
Shamima Rahman
- 15.00 - 15.30 Fenfluramine: a possible treatment for acute repetitive seizures?
Lieven Lagae
- 15.30 - 16.00 The promise of new valproic acid amide derivatives in status epilepticus
Meir Bialer
- 16.00 - 16.30 Propofol prodrug for the treatment of acute repetitive seizures
Mike Rogawski
- 14.30 - 16.30** **Parallel session: Workshop - Data blitz - EEG, basic aspects and experimental treatments**
Seminar suite
Chairs: Rob Wykes, David Henshall
International panel: Chandrashekar Agrawal, Majid Gaffar
- O-13** Electrographic predictors of successful weaning from IV anesthetics in refractory status epilepticus
Daniel B. Rubin, Brigid Angelini, Maryum Shoukat, Manohar Ghanta, J. Valdery Moura, Jin Jing, Sahar Zafar, M. Brandon Westover, Sydney Cash, Eric Rosenthal (Boston, United States)
- O-14** How and whom to monitor for seizures in an intensive care unit: a systematic review and meta-analysis
Chusak Limotai, Atiporn Ingsathit, Kunlawat Thadanipon, Mark McEvoy, John Attia, Ammarin Thakkinstian (Bangkok, Thailand; Newcastle, Australia)
- O-15** Interaction of GABAA and GABAB antagonists after status epilepticus in immature rats
Pavel Mares, Hana Kubova (Prague, Czech Republic)
- O-16** The proposed multimodal mechanism of action of cannabidiol (CBD) in epilepsy: Modulation of intracellular calcium and adenosine-mediated signalling
Colin G Stott, Kathryn Nichol, Nicholas A Jones, Royston A Gray, Michaël Bazelot, Benjamin J Whalley (Cambridge, UK; Carlsbad, USA)
- O-17** Drug-drug interaction studies with coadministration of cannabidiol (CBD) and Clobazam, Valproate, Stiripentol or Midazolam in healthy volunteers and adults with epilepsy
David Critchley, Jerzy Szaflarski, Philip Patsalos, Barry Gidal, Kevan VanLandingham, Gilmour Morrison (Cambridge, UK; University of Alabama at Birmingham, USA; London, UK; Madison, USA; Carlsbad, USA)

- O-18** NADPH oxidase inhibition modifies antiepileptogenesis and chronic epilepsy
Tawfeeq Shekh-Ahmad, Andreas Lieb, Stjepana Kovac, Lukas Gola, Andrey Y. Abramov, Matthew Walker (London, United Kingdom; Muenster, Germany)
- O-19** Acute reduction of the Extracellular Trans-Synaptic Protein LGI1 increases network excitability
Eleonora Lugarà, Marco Leite, Elodie Chabrol, Gabriele Lignani, Matthew C. Walker (London, UK)
- O-20** Argonaute-2 sequencing of rodent status epilepticus models identifies multiple microRNA targets for seizure suppression
Gareth Morris, Morten Veno, Cristina Reschke, Sebastian Bauer, Yan Yan, Tobias Engel, R Jereon Pasterkamp, Jochen HM Prehn, Stephanie Schorge, Felix Rosenow, Jorgen Kjems, David C Henshall (Dublin, Ireland; London, United Kingdom; Aarhus, Denmark; Marburg, Germany; Frankfurt am Main, Germany; Utrecht, Netherlands)
- O-21** Glio-neuronal imbalance in a stem cell-derived model of Tuberous Sclerosis Complex
Paula Rocktaeschel, Arjune Sen, Zameel Cader (Oxford, United Kingdom)
- O-22** Efficacy of intranasal Allopregnanolone in a mouse seizure model
Dorota Zolkowska, Michael A. Rogawski (Sacramento, United States)
- O-23** Anticonvulsant and neuroprotective effects of delayed treatment with Midazolam in a rodent model of organophosphate exposure
Jay Spampanato, Wendy Pouliot, Bonnie Roach, Melissa Smolik, F. Edward Dudekn(Salt Lake City, United States)
- O-24** Rapid intranasal delivery of diazepam utilizing prodrug/enzyme formulations: a promising drug delivery strategy for outpatient treatment of seizure emergencies
Davin Rautiola, Patricia D. Maglalang, Narsihmulu Cheryala, Kathryn M. Nelson, Gunda I. Georg, Jared M. Fine, Aleta L. Svitak, Katherine A. Faltsek, Leah R. Hanson, Usha Mishra, Lisa D. Coles, James C. Cloyd, Ronald A. Siegel (Minneapolis, United States)

16.30 - 17.00 **Valedictum**
 Wellcome auditorium
 Simon Shorvon, Eugen Trinkka, Matthew Walter

End of Colloquium and farewell reception

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and support to families
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ZIL/NP/19/016b Date of preparation: March 2019

P01

Novel Use of the 'Photosensitivity Model of Epilepsy' to Identify the Rapidity of Anti-Epileptic Drug (AED) CNS Penetration: Implications for Future Choice in iv Treatment of Status Epilepticus (SE)

Ronald Reed, William Rosenfeld, Susan Lippmann, Dorothee Kasteleijn Nolst Trenite (Morgantown, United States)

P02

Possible epigenetic regulatory effect of dysregulated circular RNAs in epilepsy

Woo-jin Lee, Hang-Sang Lee, Hye-Rim Shin, Eun-Young Kim, Hyoshin Son, Yong-Won Shin, Hyeyoun Chang, Soon-Tae Lee, Kyung-Il Park, Kon Chu, Sang Kun Lee (Seoul, South Korea)

P03

Two Russian cases of malignant migrating partial seizures of infancy due to KCNT1 mutations

Alexey Kholin, Inessa Fedonyuk, Anna Antonets, Ilya Komar'kov, Elena Il'ina, Nikolay Zavadenko (Moscow, Russian Federation)

P04

Characterisation of an infantile rat model of de novo status epilepticus: long-term outcomes

Geatano Terrone, Rossella Di Sapia, Alessia Salamone, Ilaria Craparotta, Nosaibeh R. Zaniani, Daniele Tolomeo, Edoardo Micotti, Sergio Marchini, Teresa Ravizza, Annamaria Vezzani (Milano, Italy)

P05

Paediatric Status Epilepticus: identification of prognostic factors using the new ILAE classification

Nicola Pietrafusa, Marina Trivisano, Luca De Palma, Marcello Bellusci, Lucia Fusco, Simona Cappelletti, Federico Vigeveno, Nicola Specchio (Rome, Italy)

P06

Some epidemiological aspects of status epilepticus in the female epilepsy

Svetlana Kravtsova, Michael Aleksandrov, Galina Odintsova, Alexey Ulitin¹Russian (St. Petersburg, Russian Federation)

P07

Status epilepticus; Experience in our intensive care unit since 2014

Luisa M Charco-Roca, Alberto Grande-Martín, Jose M Jimenez-Vizueté, Ramón Peyró-García, Pedro M Canales-Lara, Carlos Martínez-Villar, Llanos Sánchez-López (Albacete, Spain)

P08

Evaluation of our Psychogenic non-epileptic seizure status

İbrahim Bora, Aylin Bican Demir (University, Bursa, Turkey)

P09

Development of Status Epilepticus Fast Track

Sineenard Pranboon, Somsak Tiamkao (Khon Kaen, Thailand)

P10**Structural findings in patients with pharmacoresistant temporal epilepsy after anterior temporal lobectomy with a history of status epilepticus**

MD Valery Bersnev, PhD Svetlana Kravtsova, PhD Tamara Stepanova, MD Vugar Kasumov, MD Olga Gaykova, PhD Galina Odintsova, PhD Natalia Yaremenko, PhD Ksenia Zagorodnikova, Dr Daria Sitovskaya, MD Aleksey Ulitin, MD Yulia Zabrodskaya (St. Petersburg, Russian Federation)

P11**Usefulness of the brain perfusion SPECT in the diagnosis of nonconvulsive status epilepticus**

Sonia Jaraba Armas, Gabriel Reynes, Jacint Sala, Jordi Pedro, Misericordia Veciana, Júlia Miró, Oriol Puig, Jaume Mora, Mercè Falip (Barcelona, Spain)

P12**Non-convulsive status epilepticus in acute alcoholic poisoning**

Ekaterina Povaliuikhina, MD Michail Aleksandrov, PhD Tatyana Aleksandrova, MD Aleksey Ulitin (Saint-Petersburg, Russian Federation)

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References:

1. Kawai K et al. *Epileptic Disord.* 2017; 19(3):1-12.
2. Orosz I et al. *Epilepsia.* 2014 Oct; 55(10):1576-1584.
3. Data on File, LivaNova, Houston, TX.

ABSTRACTS

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O-01

Epidemiology of status epilepticus in adults: data on two population based studies in Eastern FinlandAnne-Mari Kantanen¹, Joni Sairanen¹, Reetta Kälviäinen^{1,2}¹Epilepsy Center, Neurocenter, Kuopio University Hospital, Kuopio, Finland, ²Institute of Clinical Medicine, University of Eastern Finland, Kuopio, Finland

Background: To determine the incidence of status epilepticus (SE) from the emergency medical service (EMS) call, to early phase of prolonged seizures lasting over 5 minutes to intensive care unit (ICU) treated refractory status epilepticus (RSE) and super-refractory status epilepticus (SRSE) in two population based studies in Eastern Finland.

Methods: We combined the data of two different studies conducted in Kuopio University Hospital (KUH) catchment area during the years of 2010 - 2015 to collect population based epidemiological data on early SE, RSE and SRSE. First we conducted a retrospective study on the incidence and outcome of ICU treated RSE and SRSE in adult population (> 16 years) in KUH special care responsibility area (840 000 inhabitants) from Jan 1., 2010 to 31. Dec, 2012. Secondly we conducted a prospective study of acute seizures and treatment delays using the ILAE new criteria for prolonged seizures lasting over 5 minutes in adult (> 16 years) patients in KUH municipality district (North Savo, 250 000 inhabitants) between March 23 and December 31, 2015.

Results: Local EMS co-ordinated by KUH are contacted due seizure 340 times per 100 000 inhabitants annually. In the study of early SE (seizures lasting over 5 minutes) we identified 151 consecutive episodes during the 9 months period in a population of 250 000 corresponding to an annual incidence of 80/100 000. In this prospective study 7.3%(5.8/100 000) of the seizures became refractory of which 64% (3.6/100 000) were treated with general anaesthesia in the ICU and 1.3% (1.0/100 000) as SRSE. In our earlier retrospective study on ICU treated RSE and SRSE we identified 75 RSE patients and 21% treated as SRSE in a population of 840 000 in three years resulting in an annual incidence of ICU treated RSE 3.0/100 000 and 0.6/100 000 for SRSE.

Conclusions: We conclude that the incidence of code seizure EMS calls for any type of seizure is 340/100 000, early SE (seizures lasting over 5 minutes) 80/100 000, and RSE 5.8/100 000, ICU treated RSE 3.0 – 3.6 /100 000 and SRSE 0.6 – 1.0/100 000.

O-02

30-Day Re-admission After Status Epilepticus in Unites States: Insights From Nationwide Re-admission DatabaseMonica B. Dhakar¹, David Thurman¹, Hiba A. Haider¹, Andres R. Rodriguez¹, Nathalie Jette², Edward Faught¹¹Emory University School Of Medicine, Atlanta, United States, ²Icahn School of Medicine at Mount Sinai Hospital, New York, United States

Background: Thirty-day readmission rates have increasingly gained importance as a quality metric for hospitals. Unplanned readmissions are associated with increased health care expenditure. However, there is paucity of data on 30-day readmission rates in patients with epilepsy, particularly those admitted for status epilepticus (SE). SE is often associated with prolonged hospitalization, multiple comorbidities, and cognitive deficits, all of which make these patients extremely vulnerable to repeated hospitalizations. The objective of this study was to determine the incidence, causes, predictors reasons, and costs of 30-day readmissions in patients admitted with SE from a large representative United States (US) cohort.

Methods: Adult (age ≥18 years) patients hospitalized with the primary diagnosis of SE (International Classification of Diseases-Ninth Revision-CM codes 345.2 or 345.3) between January 2013 and September 2015 who survived the index hospitalization were identified using the Nationwide Readmissions Database. Incidence, causes, and costs of 30-day readmissions were analyzed. Multivariable logistic regression model was used to identify independent predictors of 30-day readmissions.

Results: Of 42,232 patients with index SE, 6,372 (15.0%) were readmitted within 30 days. Intracranial hemorrhage (odds ratio [OR], 1.56; 95% confidence interval [CI], 1.12–2.18), psychosis (OR, 1.26, 95% CI, 1.05- 1.50), diabetes mellitus (OR, 1.12, 95% CI, 1.00- 1.25), chronic kidney disease (OR, 1.50, 95% CI, 1.31- 1.72), chronic liver disease (OR, 1.51; 95% CI, 1.24–1.84), >3 Elixhauser comorbidities (OR, 1.18; 95% CI, 1.06–1.31), length of stay >4 days during index hospitalization (OR, 1.41; 95%, CI, 1.26–1.56) and discharge to skilled nursing facility (OR, 1.14; 95% CI, 1.01–1.28) were independent predictors of 30-day readmission. The most common reason for readmission was convulsion/epilepsy (45.1%). Other non-epilepsy related readmissions were due to medical conditions; infection (9.7%), other CNS conditions (7.8%), respiratory disorders (5.1%), gastro-intestinal conditions (4.7%) and psychiatric illness (4.2%). Median length of stay and costs of readmission were 4 days (interquartile

range, 2–7 days) and \$7,882 (interquartile range, \$4,649–15,012), respectively.

Conclusions: Thirty-day readmissions after status epilepticus occur in 15% of patients. Majority of these are related to recurrent seizures. Readmitted patients were more likely to have multiple comorbidities, longer length of stay, and discharge to skilled nursing home facility. Awareness of these predictors can help identify and target high-risk patients for interventions to reduce readmissions and costs.

O-03

Status Epilepticus Mortality Score after 30 Days of Hospital Discharge: Development and Validation Using Competing Risks Analysis

Somsak Tiamkao^{1,2}, Prapassara Sirikarn^{2,3}, Porjai Pattanittum³, Integrated Epilepsy Research Group²

¹Division of Neurology, Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand, ²Integrated Epilepsy Research Group, Khon Kaen University, Khon Kaen, Thailand, ³Department of Epidemiology and Biostatistics, Faculty of Public Health, Khon Kaen University, Khon Kaen, Thailand

Background: Status epilepticus (SE) is an emergency neurological disorder that affects quality of life and associates with high mortality risk. Three scores developed to predict the risk of in-hospital death but the result of applying the score with mortality after discharge was poor discrimination. This study aims to develop and validate the simple risk score for long-term mortality in SE patients.

Methods: This retrospective cohort study conducted using the data of SE patients from the national data of Universal Coverage Scheme in Thailand between fiscal year 2005 to 2015 and followed-up to 2016. The patients who died in hospital, or died within 30 days after discharge were excluded. Data was randomly split into derivation and validation set. A proportional hazards model for the sub-distribution of competing risks model was fitted with backward stepwise. The coefficients from the model were used for setting up the points-based scorings system. Discrimination ability of the model was evaluated by time-dependent receiver operating characteristic (ROC) curve.

Results: 20,792 SE patients (first day of life to 99 years at 1st admission) were randomly separated into 2 groups: 13,910 for developing and 6,882 for validating. Nine predictors were selected into the final model by sub-distribution hazard model and it was used in developing the scoring

system; age (0-19 points), male (2 point), brain tumor (12 point), stroke (3 point), cancer (11 point), diabetes (3 point), chronic kidney disease (5 point), pneumonia (5 point), and urinary tract infection (4 point). The possible total score ranged from zero to 64 and the cumulative incidence function was to determine the probability of event for each total score in the first year to 10-year after the first episode of SE. The area under the ROC curve (AUC) of the first to last time point ranged from 0.760 to 0.738.

Conclusions: The nine-factor risk score for predicting 10-year mortality in SE patients was developed. The sensitivity analyses regarding selection procedures found that backward closely resembles to backward stepwise. Further studies could focus on external validity and adding of types and duration of seizure.

O-04

Cause of Death in Status Epilepticus Patients

Somsak Tiamkao^{1,3}, Prapassara Sirikarn^{2,3}, Porjai Pattanittum³, Integrated Epilepsy Research Group³

¹Division of Neurology, Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand, ²Department of Epidemiology and Biostatistics, Faculty of Public Health, Khon Kaen University, Khon Kaen, Thailand, ³Integrated Epilepsy Research Group, Khon Kaen University, Khon Kaen, Thailand

Background: Status epilepticus (SE) is a neurological disorder that effects to the high risk of death. In fact, the causes of death in SE is not directly due to seizure, but also indirect causes: suicide, complications, and underlying diseases of an individual patient. Even several studies reported the mortality in SE, but lack of reporting the causes of death in long term. Thus, this study aims to describe the mortality rate and the causes of death in SE patients.

Methods: This is a retrospective cohort study using the data collected in the national data of the Universal Coverage Scheme (USC) in Thailand during the fiscal year 2005 – 2015. Patients who admitted to hospitals and diagnosed as SE were included. The vital status of SE patients was linked with the Ministry of the Interior and was classified into three phases: in-hospital, short-term, and long-term. **Results:** Among 24,802 SE patients, 1,861 (7.5%) died in hospital, 1,910 (7.7%) died within 30 days after hospital discharge, and 4,906 (19.8%) died after 30 days. Of 8,677 SE patients, they died because of seizure (10.1%, 95%CI: 3.4% - 10.7%), accidents (5.0%, 95%CI: 4.6% - 5.5%), suicides (0.6%, 95%CI: 0.5% - 0.8%), SE complications

(33.3%, 95%CI: 32.3% - 34.3%), comorbid conditions (24.3%, 95%CI: 23.4% - 25.2%), other causes (18.8%, 95%CI: 18.0% - 19.7%), and unknown causes of death (7.9%, 95%CI: 7.4% - 8.5%). In-hospital death, SE complications (45.8%, 95%CI: 43.6% - 48.1%), seizure (19.6%, 95%CI: 17.8% - 21.5%), and comorbidities (15.3%, 95%CI: 13.7% - 17.0%) were three common causes of death. While the common causes in short-term and long-term mortality were SE complications (27.7%, 95%CI: 25.7% - 29.8% and 30.7%, 95%CI: 29.4% - 32.0%), comorbidities (28.0%, 95%CI: 26.0% - 30.1% and 26.2%, 95%CI: 25.0% - 27.4%), and other causes (22.5%, 95%CI: 20.6% - 24.4% and 22.4%, 95%CI: 21.2% - 23.6%).

Conclusion: SE complications were the most common cause of death in SE patients for all of three periods.

0-05

Factors related to the development of mesial temporal sclerosis after status epilepticus

Estevo Santamarina, Silvana Sarria, Laura Abraira, Elena Fonseca, Xavier Salas - Puig, Manuel Quintana, Manuel Toledo

Hospital Vall Hebron, Barcelona, Spain

Background: There are relatively little data regarding mesial temporal sclerosis (MTS) as a sequela of prolonged seizure activity. This finding may be important to study epileptogenesis in status epilepticus (SE). Our aim is to study all factors related to the development of MTS in SE patients.

Methods: All our patients >16yo experiencing SE are prospectively recorded in a registry since 2011. The variables collected include demographics, etiology, SE type, refractoriness/duration, EEG pattern and neuroimaging. We selected those patients with no previous history of epilepsy and MRI during follow-up; we analyzed all factors in relation to development of MTS.

Results: We evaluated 52 patients. Mean age: 59yo; 27(51.9%) male. 25(48.1%) were without prominent motor symptoms. Median mSTESS: 3. Regarding etiology: 32(61.5%) were acute symptomatic, 9(17.3%) remote symptomatic, 8(15.4%) progressive symptomatic and 3(5.8%) cryptogenic. LPDs were present in 14(26.9%). 29(55.8%) were considered refractory. 24 patients had a brain injury affecting temporal lobe, and 28 had other affected lobes or no brain injury. MRI was performed between 1.5 and 24 months after SE. MTS was observed in 19(36.5%). When analyzing its development, MTS

was clearly more frequent in brain lesions affecting the temporal lobe ($p=0.0001$), with some etiologies such a remote cerebrovascular disease/brain injury ($p=0.001$) or an acute CNS infection ($p=0.014$), with higher EMSE scores ($p=0.011$), and when LPDs were present ($p=0.002$); furthermore, we observed a tendency in older patients ($p=0.089$). After a multivariate analysis, the factors predicting the development of MTS were the presence of a lesion in temporal lobe ($p=0.003$), and specific etiologies: a remote cerebrovascular lesion or traumatic brain injury ($p=0.002$) and an acute CNS infection ($p=0.031$). In 43 patients, an acute MRI was also performed, 19 (44.2%) showed changes related to SE in DWR and 30 (69.8%) in T2; when MRI acute changes were included in regression, the presence of a lesion in temporal lobe ($p=0.046$) and a remote vascular or traumatic lesion ($p=0.016$) remained as predictors of MTS, in addition to the finding of acute post-SE changes in DWR ($p=0.091$).

Conclusion: In SE patients, the development of MTS was related with specific etiologies and the location of the brain insult.

0-06

Neurological outcome of post-anoxic refractory status epilepticus after aggressive treatment

Simone Beretta¹, Anna Coppo², Elisa Bianchi³, Clara Zanchi¹, Davide Carone¹, Andrea Stabile¹, Giada Padovano¹, Endrit Sulmina², Graziella Bogliun¹, Giuseppe Foti², Carlo Ferrarese¹, Ettore Beghi³, Leonello Avalli³

¹Department of Neurology, San Gerardo Hospital, University Of Milano Bicocca, Monza, Italy, ²Department of Intensive Care, San Gerardo Hospital, University Of Milano Bicocca, Monza, Italy, ³IRCCS Mario Negri Institute for Pharmacological Research, Milano, Italy

Background: Refractory status epilepticus (RSE) occurs in up to 30% of patients following resuscitation after cardiac arrest. The impact of aggressive treatment of post-anoxic RSE on long-term neurological outcome remains uncertain. We investigated neurological outcome of cardiac arrest patients with RSE treated with a standardized aggressive protocol with anti-epileptic drugs and anesthetics, compared to patients with other EEG patterns.

Methods: Prospective cohort study of 166 consecutive patients with cardiac arrest in coma, stratified according to four independent EEG patterns (benign; RSE; generalized periodic discharges, GPDs; malignant non-epileptiform) and multi-modal prognostic indicators. Primary outcomes were survival and cerebral performance category (CPC) at

6 months.

Results: RSE occurred in 36 patients (21.7%) and was treated with an aggressive standardized protocol as long as multi-modal prognostic indicators were not unfavorable. RSE started after 3 +/- 2.3 days after cardiac arrest and lasted 4.7 +/- 4.3 days. A benign EEG pattern was recorded in 76 patients (45.8%), a periodic pattern (GPDs) in 13 patients (7.8%) and a malignant non-epileptiform EEG pattern in 41 patients (24.7%). The four EEG patterns were highly associated to different prognostic indicators (low flow time, clinical motor seizures, N20 responses, NSE, neuroimaging). Survival and good neurological outcome (CPC 1 or 2) at 6 months were 72.4% and 71.1% for benign EEG pattern, 54.3% and 44.4% for RSE, 15.4% and 0% for GPDs and 2.4% and 0% for malignant non-epileptiform EEG pattern, respectively.

Conclusions: Aggressive and prolonged treatment of RSE may be justified in cardiac arrest patients with favorable multi-modal prognostic indicators.

O-07

Prolonged Seizures in Children

Clodagh Mitchell¹, Libby Dickson¹, Paul Leonard², Celia Brand², Ailsa McLellan², Jay Shetty²

¹University Of Edinburgh, Edinburgh, United Kingdom, ²Royal Hospital for Sick Children, Edinburgh, United Kingdom

Background: Prolonged seizures (PS) in children carry significant risk of morbidity and mortality. Previous work has predominantly focused on status epilepticus ≥ 30 min but a new ILAE definition has been produced following evidence that seizures ≥ 5 min are associated with negative outcomes. There has been increasing effort by clinicians and epilepsy specialist nurses to manage PS effectively through benzodiazepines, education and training. This study aims to provide population-based data on children presenting with PS and their outcomes.

Methods: All children presenting to accident and emergency (A+E) between 2011-2017 from a Scottish Children's hospital were identified (capture-recapture method with multiple datasets). Data was collated from electronic health records; including patient demographics, clinical characteristics, acute seizure management and outcomes. This data can be used to study long-term outcomes, including educational outcome, through national data linkage systems.

Results: There were 666 children (1234 seizure episodes). These accounted for 0.38% (95% CI (0.34-0.42%)) of A+E admissions. Yearly prevalence rate was 0.8 per 1000 children. The median age was 3.65 years (range 0-20 years) and 54% of children were male (95% CI (53.1-60.7%)). The median seizure duration was 10 minutes (range 5 to 195 minutes). PS incidence increased at the extremes of socioeconomic status and relationship with distance from A+E can be determined. Seizure duration, mortality and requirement for ventilatory support decreased compared to historical data. Data highlighted children with epilepsy and those in specialist education as two particularly at risk groups for recurrent prolonged seizures. There was a lower likelihood of hospital admission where buccal midazolam was administered.

Conclusions: Adverse outcomes have decreased and the use of buccal midazolam is promising. Identifying high-risk groups provides opportunity for early intervention. This data forms the basis for extensive evaluation of acute seizure management and monitoring long-term outcomes.

O-08

Long-term Safety and Efficacy of Add-on Cannabidiol (CBD) Treatment in Patients with Lennox Gastaut Syndrome in an Open-label Extension Trial (GWPCARE5)

Richard Chin¹, Anup Patel², Antonio Gil-Nagel³, Wendy Mitchell⁴, M Scott Perry⁵, Arie Weinstock⁶, Lauren Whyte⁷, Kevan VanLandingham⁸

¹Royal Hospital For Sick Children, Edinburgh, UK, ²Nationwide Children's Hospital, Columbus, USA, ³Hospital Ruber International, Madrid, Spain, ⁴Children's Hospital Los Angeles, Los Angeles, USA, ⁵Cook Children's Medical Center, Fort Worth, USA, ⁶Oishei Children's Hospital, Buffalo, USA, ⁷GW Research Ltd, Cambridge, UK, ⁸Greenwich Biosciences, Inc., Carlsbad, USA

Background: Lennox-Gastaut syndrome (LGS) is a rare epileptic encephalopathy that is often treatment-resistant. The efficacy of cannabidiol (CBD) was demonstrated with an acceptable safety profile in two Phase 3 randomised controlled trials (RCTs): GWPCARE3 (NCT02224560) and GWPCARE4 (NCT02224690). A second interim analysis of the open-label extension (OLE) of the two RCTs was conducted to assess long-term safety and efficacy of add-on CBD treatment in patients with LGS.

Methods: Patients who completed a 14-week, double-blind, randomised controlled trial (GWPCARE3/NCT02224560; GWPCARE4/NCT02224690) could enter this OLE trial

(GWPCARE5/NCT02224573). Patients received GW Pharmaceuticals' formulation of plant-derived highly purified CBD in oral solution (100 mg/mL) for ≤ 3 years. Primary endpoint was safety. Secondary endpoints were drop and total seizure frequency, and Subject/Caregiver Global Impression of Change (S/CGIC).

Results: Overall, 99% (366/368) of eligible patients with LGS entered the OLE trial. Median follow up was 61 weeks (3 days to 87 weeks); 88 patients (24%) withdrew. Mean age: 16 years; 33% ≥ 18 years; 54% male. Baseline median seizure frequency/28 days: 80 drop seizures; 168 total seizures. During the extended follow up, adverse event (AE) incidence: 94%; serious AE incidence: 33%; 11% discontinued owing to AEs. Most common AEs ($\geq 20\%$): diarrhoea, convulsion, somnolence, pyrexia, vomiting and decreased appetite. Forty-seven patients (13%) had elevations in liver transaminases $>3\times$ upper limit of normal; 35 (74%) were taking concomitant valproate. There were 5 deaths; none deemed treatment-related by the investigator(s). Median percentage reductions in seizure frequency (12-week windows over 72 weeks): 48–70% for drop seizures; 48–63% for total seizures. Approximately 88% of patients/caregivers reported an improvement in overall condition on the S/CGIC at Weeks 24 and 48.

Conclusions: Long-term add-on CBD treatment had a similar AE profile to that observed in the core studies at 14 weeks. Reductions in drop and total seizure frequency and improvements in overall condition were maintained through 72 weeks.

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O-09

Serum neurofilament light chain as a prognostic marker in post-anoxic encephalopathy

Giulio Disanto¹, Chiara Prosperetti¹, Claudio Gobbi¹, Christian Barro², Zuzanna Michalak², Tiziano Cassina³, Jens Kuhle², Gabriele Casso³, Pamela Agazzi¹

¹Neurocentre of Southern Switzerland, Lugano, Switzerland, ²Neurologic Clinic and Policlinic, Departments of Medicine, Biomedicine and Clinical Research, University Hospital Basel, University of Basel, Basel, Switzerland, ³Cardiocentro Ticino, Lugano, Switzerland

Functional outcome in patients suffering from post-anoxic encephalopathy after cardiac arrest (CA) often remains unclear and there is a strong need of new prognostication measures. We aimed at investigating serum neurofilament

light chain (NfL) concentration in patients with a post-anoxic encephalopathy after CA and its prognostic potential.

Serum samples were prospectively collected at different time points after CA in consecutive patients admitted to the intensive care unit (ICU) of Ticino Cardiocentre (Lugano Switzerland) between June 2017 and March 2018. Serum NfL concentration was measured using a single molecule array (SIMOA) assay. The association of NfL levels with time to return of spontaneous circulation (ROSC), serum neuronal specific enolase (NSE) concentration, time between CA and sample collection, EEG pattern and clinical outcome (death status at one month) were explored.

Fourteen patients experiencing 15 CAs were included the study (median age=58 (57-68) years, 8 males). Median serum NfL concentration was 1,027.0 (25.5-6033.7) pg/ml. There were positive associations between serum NfL and time to ROSC ($\rho=0.60$, $p<0.0001$), NSE concentration ($\rho=0.76$, $p<0.0001$) and severity of brain damage as estimated by EEG, with the highest concentrations measured in patients with suppressed electrical activity (14,954.0 [9,006.0-25,364.0] pg/ml). NfL concentration remained high in samples collected up to 17 days after CA. Median NfL levels were higher among dead than alive patients at one month (6,401.7 [3,768.5-15,573.3] vs 25.5 [25.2-75.4] pg/ml). High NfL levels performed better than NSE in predicting death status at one month (NfL AUC=0.98, 95CI%=0.94-1.00; NSE AUC=0.80, 95%CI=0.67-0.94).

These results support the potential inclusion of serum NfL in the battery of prognostication measures to be used in patients suffering from post-anoxic encephalopathy in ICU settings.

O-10

Responsive Neurostimulation Therapy for Super-Refractory Autoimmune Epilepsy

Anteneh Feyissa¹, William Tatum¹, Jeffrey Britton²

¹Mayo Clinic, Jacksonville, United States, ²Mayo Clinic, Rochester, United States

Background: Immunotherapy remains the cornerstone for treatment of autoimmune epilepsy; however, some remain super-refractory despite immunotherapy and anti-seizure medications (ASMs).

Methods: Case-series study of two patients with super-refractory AE treated with bilateral hippocampal responsive

neurostimulation (RNS).

Results: Case 1: A 37 year-old woman presented with frequent (5-8/day) focal seizures with flushing and disabling chest pain of 4 years. Seizures are refractory to intravenous methylprednisolone and immunoglobulin and 9 ASMs. Serum autoimmune epilepsy panel was positive for Glutamic acid decarboxylase 65 (GAD65) antibody (250mg/dL). Brain MRI showed left mesial temporal sclerosis (MTS) and fluorodeoxyglucose positron emission tomography (fdg-PET) showed bitemporal hypometabolism. Evaluation for occult malignancy was negative. Bilateral independent temporal seizures were recorded. She was treated with RNS utilizing bi-hippocampal electrodes. Right hippocampal onset seizures were aborted within 8 weeks, however left hippocampal onset seizures were only reduced by 25%. At 18 months, she continued to experience seizures, albeit at reduced frequency.

Case 2: A 39 year-old woman presented with frequent focal and bilateral tonic clonic seizures. CSF was inflammatory but neuroimmunology panel was negative. Seizures are refractory to intravenous methylprednisolone and immunoglobulin, plasma exchange, Rituximab, Cyclophosphamide, and Azathioprine, 11 ASMs, and vagus nerve stimulation therapy. Brain MRI showed bilateral MTS. Screening for occult was unrevealing. Bilateral independent temporal seizures were recorded, and she was implanted with bi-hippocampal RNS electrodes. Within 8 weeks, seizure frequency was reduced by over 50%. Further, the RNS data disclosed catamenial clustering and led to the initiation of progesterone. At 6 months follow-up, she reported significant seizure reduction.

Conclusions: RNS has a role in the treatment of super-refractory autoimmune epilepsy. RNS helps track seizure burden objectively and may inform anti-seizure medication optimization in this patient population.

O-11

Updated Data on the Tocilizumab Treatment in New Onset Refractory Status Epilepticus

Hyoshin Son, Soon-Tae Lee, Hye-Rim Shin, Eun-Young Kim¹, Woo-Jin Lee, Kon Chu, Kyung-Il Park, Sang Kun Lee

Department of Neurology, Seoul National University Hospital, Seoul, South Korea

Background: New onset refractory status epilepticus (NORSE) is defined by new onset status epilepticus (SE), showing no response to at least 2 anti-epileptic drugs (AEDs) without evidence of other structural, toxic, or

metabolic causes in patients who have been otherwise previously healthy. As no clear etiology has been established for NORSE, autoimmune or paraneoplastic causes account for the majority of NORSE cases with an identifiable cause. Even though immunotherapies including steroid, immunoglobulin, and rituximab have been tried to treat NORSE, approximately 60% of the patients had poor functional outcomes, suggesting need of the next line of immunotherapy. With updated data on the tocilizumab treatment in NORSE patients, we investigated the therapeutic potential of the tocilizumab, interleukin-6 receptor inhibitor, as new candidate of immunotherapy for NORSE.

Methods: In this study, updated data on two additional NORSE patients were analyzed to the previous data published. In a prospective cohort for autoimmune encephalitis since June 1, 2012, of which patients who have been admitted to Seoul National University, the patients who were diagnosed with NORSE with poor response to conventional immune therapy including steroid, immunoglobulin, and rituximab and treated with tocilizumab from August 2015 to November 2018 were subjected to further analysis.

Results: Compared to the previous data of 7 SE patients, 7 out of 9 SE patients showed cessation of SE with a median interval of 5 days from the initiation of treatment. According to our data, patients who responded to tocilizumab tended to show either clinical or electrophysiological improvement at most within the second cycle of treatment, which means early response to treatment. Two patients experienced infection as adverse event after tocilizumab treatment, and one patient on updated data showed no response to tocilizumab even after two cycles of treatment.

Conclusions: Tocilizumab treatment resulted in cessation of SE in 7 out of 9 patients according to our results. Therapeutic effects of tocilizumab on SE patients who do not show definite response to conventional immunotherapy are to be further studied with alternative immunologic pathway, and further prospective study with larger number of patients is warranted.

0-12

Combination therapy of immunoglobulin, Rituximab, and Tocilizumab in treating acute autoimmune encephalitis

Woo-jin Lee, Han-Sang Lee, Hye-Rin Shin, Eun-Young Kim, Hyoshin Son, Yong-Won Shin, Hye-yeon Chang, Soon-Tae Lee, Kyung-Il Park, Kon Chu, Sang Kun Lee

Seoul National University Hospital, Seoul, South Korea

Background: A considerable portion of autoimmune encephalitis (AE) does not respond to conventional immunotherapies and subsequently have poor outcomes. Tocilizumab, an anti-interleukin-6 antibody, has some effect on treating AE refractory to first-line immunotherapies and Rituximab. We aimed to determine the efficacy of the combination therapy of immunoglobulin (\pm steroid), Rituximab, and Tocilizumab (IsRT) in treating acute AE over conventional treatment options.

Methods: This institutional cohort included seventy-nine consecutive patients with antibody-proven AE. Acute treatment regimens were categorized as IsRT, IsR, and Is. Patients' clinical severity was assessed at every two weeks for the first three months, at every month for the next three months, and then at every three months, using the Clinical Assessment Scales in Autoimmune Encephalitis (CASE, 9 clinical items, score range 0–27). Outcomes were categorized into excellent (CASE scores 0–4), moderate (CASE scores 5–19), and poor (CASE scores 20–27) at the last follow-up. The 3-month clinical responsiveness to immunotherapies was designated as the early outcome parameter and defined as the major improvement of CASE scores (≥ 4) within the first 3 months.

Result: As acute treatment regimens, 33 patients received IsRT, 32 received IsR, and 14 received Is. Compared to the conventional treatment groups (IsR and Is), IsRT group exhibited higher initial CASE scores, higher level of CSF leukocyte, and more frequent use of ventilator care. 3-months clinical responsiveness was the single most powerful parameter associated with excellent or poor final clinical outcomes. Multivariate analysis showed that along with the initial CASE score, IsRT regimen was associated with higher frequency of achieving clinical responsiveness at 3 months. Frequency of serious adverse effects were comparable among the treatment regimens.

Conclusion: Combination treatment of immunoglobulin, Rituximab, and Tocilizumab in the acute phase of AE might enhance the clinical responsiveness to immunotherapy and therefore be a good treatment strategy.

0-13

Electrographic Predictors of Successful Weaning from IV Anesthetics in Refractory Status Epilepticus

Daniel B. Rubin, Brigid Angelini, Maryum Shoukat, Manohar Ghanta, J. Valdery Moura, Jin Jing, Sahar Zafar, M. Brandon Westover, Sydney Cash, Eric Rosenthal

Massachusetts General Hospital, Harvard Medical School, Boston, United States

Parallel session: Data blitz – EEG, basic aspects and experimental treatments, April 9, 2019, 14:30 - 16:30

Background: Intravenous third-line anesthetic agents (IV-TLA) are titrated in refractory status epilepticus (RSE) to achieve either seizure suppression or burst suppression on EEG. However, little data exist to help guide clinicians in the weaning of IV-TLA in RSE. This study sought to evaluate several quantitative measures of EEG activity during IV-TLA weaning in RSE, employing novel analytic techniques to help identify patients that may successfully wean from IV-TLA.

Methods: We identified patients diagnosed with RSE who underwent at least one IV-TLA wean, excluding patients presenting with cardiac arrest. A successful IV-TLA wean was defined as the discontinuation of an IV-TLA without the development of recurrent status epilepticus for at least 48 hours. A wean failure was defined as either recurrent status epilepticus or the resumption of IV-TLA (other than for patient comfort). Two quantitative analyses were performed: a frequency-based analysis in which the power of spectral components of the EEG signal were calculated, and a novel spatial-correlation-based analysis, in which EEG data were used to generate continuous maps of functional connectivity during each IV-TLA wean. The power and ratios of spectral components and the parameters characterizing functional network topology were then used to compare successful and unsuccessful weans. The results of these quantitative analyses were used to train a classifier to predict wean outcome.

Results: Twenty-six patients undergoing 40 anesthetic weans (18 successes, 22 failures) were identified. Quantification of signal power in discrete frequency bands revealed no significant differences between successful and unsuccessful weans. Analysis of functional connectivity measures revealed that successful IV-TLA weans were characterized by larger, more highly-clustered spatial networks of activity. Specifically, functional networks from patients undergoing successful IV-TLA weans had a significantly higher mean density, higher mean clustering coefficient, fewer independent components, and larger largest components than those from patients that failed anesthetic wean.

Conclusions: Distinct patterns of changes in the spatial networks of functional connectivity emerge during successful anesthetic weans that are absent in wean failures. Identifying EEG features that dynamically emerge during successful IV-TLA weaning may help optimize anesthetic management for RSE by preventing an unnecessary excess of wean attempts or weaning duration.

O-14

How and whom to monitor for seizures in an intensive care unit: a systematic review and meta-analysis

Chusak Limotai^{1,2,3}, Atiporn Ingsathit³, Kunlawat Thadanipon³, Mark McEvoy⁴, John Attia⁴, Ammarin Thakkinian³

¹Chulalongkorn Comprehensive Epilepsy Center of Excellence (CCEC), The Thai Red Cross Society, Bangkok, Thailand, ²Division of Neurology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, ³Section for Clinical Epidemiology and Biostatistics, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, ⁴School of Medicine and Public Health, The University of Newcastle, Newcastle, Australia

Background: Identification of patients with the greatest need for continuous EEG (cEEG) monitoring is helpful for appropriate prioritization. Neither of the previous systematic reviews provided pooled prevalence of nonconvulsive seizure (NCS)/ nonconvulsive status epilepticus (NCSE) or directly compared NCS/NCSE detection rates between EEG types. This review was aimed to pool prevalence of NCS, NCSE, and epileptiform activity (EA) detected by cEEG and routine EEG (rEEG) in critically ill and to compare detection rates among them.

Methods: Data Sources: MEDLINE (via PubMed) and SCOPUS (via Scopus) Study Selection: Any type of study was eligible if studies were done in adult critically ill, applied any type of EEG, and reported seizure rates. Case reports and case series were excluded.

Data Extraction: Data were extracted independently by 2 investigators. Separated pooling of prevalence of NCS/NCSE/EA and odds ratio (OR) of detecting outcomes among different types of EEG was performed using random-effect models. This meta-analysis followed PRISMA guidelines and also adhered to MOOSE guidelines. Quality of evidence was assessed with the Newcastle-Ottawa Quality Assessment Scale (NOS) for observational studies and Cochrane methods for randomized controlled trial studies. PROSPERO registration number is 42017072579.

Results: A total of 78 (16707 patients) and 8 studies (4894 patients) were eligible for pooling prevalence and odds ratios (ORs). For patients with mixed cause of admission, the pooled prevalence of NCS, NCSE, either NCS or NCSE (NCS/NCSE) detected by routine EEG (rEEG) was 3.1%, 6.2%, and 6.3%, respectively. The corresponding prevalence detected by continuous EEG (cEEG) monitoring was 17.9%, 9.1%, and 15.6%, respectively. In addition, the corresponding prevalence was high in post convulsive status epilepticus (CSE) (33.5%, 20.2%, and 32.9%), central nervous system (CNS) infection (23.9%, 18.1%, and 23.9%), and post cardiac arrest (20.0%, 17.3%, and 22.6%). The pooled conditional log ORs of NCS/NCSE detected by cEEG versus rEEG from studies with paired data were 2.57 (95% CI 1.11, 5.96) and pooled ORs from studies with independent data was 1.57 (95% CI 1.00, 2.47).

Conclusions: Prevalence of seizures detected by cEEG was significantly higher than with rEEG. Prevalence was particularly high in post CSE, CNS infection, and post cardiac arrest.

O-15

Interaction of GABAA and GABAB antagonists after status epilepticus in immature rats

Pavel Mares, Hana Kubova

Institute Of Physiology, Czech Academy Of Sciences, Prague, Czech Republic

Background: GABA_B receptors are among neurotransmitter systems compromised by status epilepticus (SE) in adult animals (Mangan and Lothman 1996). Recently we demonstrated that function of GABA_B system is affected by SE also in immature rats (Mareš and Kubová 2019). We continued the analysis of these changes in present series of experiments.

Methods: Lithium-pilocarpine SE was elicited in 12-day-old (P12) rat pups. Each nest consisting of 10 pups was divided into experimental (SE) and control (saline instead of pilocarpine, LiPAR groups) animals. After 90 minutes of epileptic activity all animals received paraldehyde (0.07ml/kg i.p.) to interrupt SE and decrease mortality. Low dose of pentylenetetrazol (50 mg/kg s.c.) was combined with a pretreatment with GABA_B receptor antagonist CGP46381 (10 mg/kg i.p.) in animals 15, 18, 21 and 25 days old and incidence, pattern and latency of seizures were compared between SE, LiPAR and naive groups.

Results: Naïve animals exhibited significant potentiation of convulsant action of PTZ by CGP46381 in P18 rats, similar tendency in P15 and P21 rats did not reach the level of statistical significance. In contrast, P25 animals exhibited significant anticonvulsant action of GABA_B antagonist in PTZ seizure test. Tendency to proconvulsant action was suppressed in P15 and P21 SE animals, whereas significant potentiation was found in P18 SE rats. LiPAR controls demonstrated marked potentiation in P15 and P18 rats, this effect was no longer present in P21 animals. Results in P25 groups corresponded with data from naïve animals.

Conclusions: rat pups three days after SE did not exhibit proconvulsant action of the GABA_B antagonist in contrast to LiPAR controls and naïve animals. Potentiation of PTZ convulsant action by GABA_B receptor antagonist was not present at P21 in both SE and LiPAR rats, i.e. the change of CGP46381 action took place earlier than in naïve controls. This study was supported by a grant of Czech Grant Agency No.18-09296S and a European Regional Development Fund-Project PharmaBrain No. CZ.02.1.01/0.0/0.0/16_025/0007444.

O-16

The Proposed Multimodal Mechanism of Action of Cannabidiol (CBD) in Epilepsy: Modulation of Intracellular Calcium and Adenosine-mediated Signalling

Colin G Stott¹, Kathryn Nichol², Nicholas A Jones¹, Royston A Gray¹, Michaël Bazélot¹, Benjamin J Whalley¹

¹GW Research Ltd, Cambridge, UK, ²Greenwich Biosciences, Inc., Carlsbad, USA

Background: Although commonly misrepresented, cannabidiol (CBD) does not act directly through cannabinoid receptors at physiologically achievable concentrations. CBD has shown anticonvulsant properties in non-clinical studies and antiseizure effects in clinical trials of Dravet and Lennox-Gastaut syndromes with a unique multimodal molecular target profile, distinct from other antiepileptic drugs. We present preclinical evidence summarising CBD's leading mechanisms of action in epilepsy.

Methods: Preclinical evidence suggests CBD reduces neuronal hyperexcitability through multiple mechanisms, including modulation of intracellular calcium via G protein-coupled receptor 55 (GPR55), extracellular calcium influx via transient receptor potential vanilloid type 1 (TRPV1) channels and adenosine-mediated signalling.

Results: CBD antagonises GPR55 at excitatory synapses. The inhibition of intracellular calcium release decreases excitatory currents and seizure activity. GPR55-mediated modulation of neurotransmission was potentiated in excitatory neurons and reduced in inhibitory neurons in a chronic epilepsy model. CBD potently blocked the GPR55-mediated increase of miniature excitatory postsynaptic current frequency in pyramidal neurons in both healthy and epileptic tissue. CBD did not affect the GPR55-mediated increase of excitatory neurotransmission in inhibitory neurons in healthy tissue. CBD's anticonvulsant properties were attenuated in GPR55 knockout (KO) animals.

CBD desensitises TRPV1 channels. The resultant decrease in extracellular calcium influx decreases neurotransmission. The dose-dependent CBD-mediated increase in seizure threshold seen in wild type mice was significantly attenuated in TRPV1 KO mice. Brain CBD concentrations were consistent with those required for TRPV1 activation and desensitisation irrespective of genotype.

CBD inhibits the equilibrative nucleoside transporter 1 (ENT1), reducing adenosine reuptake. The increase in extracellular adenosine reduces hyperexcitability and neurotransmission. CBD inhibited [³H] adenosine uptake into rat cortical synaptosomes at low micromolar concentrations.

Conclusions: While the precise mechanisms by which CBD exerts its anticonvulsant properties in humans remain unknown, growing preclinical evidence suggests CBD reduces neuronal hyperexcitability through a unique multimodal mechanism of action. CBD antagonises GPR55 at excitatory synapses, desensitises TRPV1 channels and inhibits adenosine reuptake.

Funding: GW Research Ltd

O-17

Drug-drug Interaction Studies with Coadministration of Cannabidiol (CBD) and Clobazam, Valproate, Stiripentol or Midazolam in Healthy Volunteers and Adults with Epilepsy

David Critchley¹, Jerzy Szaflarski², Philip Patsalos³, Barry Gidal⁴, Kevan VanLandingham⁵, Gilmour Morrison¹

¹GW Research Ltd, Cambridge, UK, ²Department of Neurology and University of Alabama at Birmingham Epilepsy Center, University of Alabama at Birmingham, USA, ³Institute of Neurology, University College London, London, UK, ⁴School of Pharmacy, University of Wisconsin-Madison, Madison, USA, ⁵Greenwich Biosciences, Inc., Carlsbad, USA

Background: Drug-drug interactions (DDIs) between cannabidiol (CBD) and commonly used antiepileptic drugs (AEDs) is of clinical interest since it is anticipated that CBD will be used concomitantly with other AEDs. We present a summary of current understanding of DDIs when CBD is coadministered with clobazam (CLB), valproate (VPA), stiripentol (STP) or CYP3A4 substrate.

Methods: Effects of multiple-dose CBD on steady-state pharmacokinetics (PK) of CLB, N-desmethyl clobazam (N-CLB), VPA, 2-propyl-4-pentenoic acid (4-ene-VPA) and STP, and multiple-dose CLB, VPA and STP on steady-state PK of CBD and metabolites were evaluated in healthy volunteers. Effects of multiple-dose CBD on steady-state PK of CLB, N-CLB, VPA and 4-ene-VPA were evaluated in patients with epilepsy. The effect of CBD on CYP3A4 activity was evaluated in healthy volunteers using midazolam (MDZ) as a probe. In all studies, GW Pharmaceuticals' formulation of plant-derived highly purified CBD in oral solution (100 mg/mL) was uptitrated over 10 days to 750 mg twice daily in healthy volunteers (20 mg/kg/day for a 75 kg subject) or 20 mg/kg/day in patients.

Results: Concomitant CBD had no relevant effect on CLB exposure but increased exposure to its active metabolite, N-CLB, in healthy volunteers (3.4 fold) and patients (2.6 fold). Conversely, concomitant CLB increased CBD (by 30%) and its active metabolite, 7-OH-CBD (by 47%). Concomitant CBD had no effect on VPA or 4-ene-VPA, and slightly increased exposure to STP (by 55%). Concomitant VPA or STP did not alter CBD or its metabolites. CBD had no effect on MDZ clearance. CBD demonstrated a safety profile consistent with previous randomised placebo-controlled trials.

Conclusions: Combination of CBD with CLB resulted in a bidirectional DDI that increased levels of active metabolites of both compounds. There was no evidence of a DDI between CBD and VPA, or any effect of CBD on CYP3A4 activity (MDZ). The slight increase of exposure to STP when coadministered with CBD is not expected to result in a clinically important DDI.

Funding: GW Research Ltd

0-18

NADPH oxidase inhibition modifies antiepileptogenesis and chronic epilepsy

Tawfeeq Shekh-Ahmad¹, Andreas Lieb¹, Stjepana Kovac^{1,2}, Lukas Gola², Andrey Y. Abramov¹, Matthew Walker¹

¹UCL Institute of Neurology, University College London, Queen Square, London, United Kingdom, ²Department of Neurology, University of Muenster, Muenster, Germany

Background: Epilepsy remains a major neurological disease with 30% of which remains refractory to drug therapy. A common sequelae of brain injury is the generation of reactive oxygen species (ROS) and induction of oxidative stress. During prolonged seizures (status epilepticus, SE), ROS are produced through activation of NADPH oxidase (NOX) via NMDA receptor activation, which contribute to seizure associated neuronal death.

Therefore, antioxidant therapies are potential therapeutic approach to counteract ROS-mediated neuronal cell death and seizures development.

Methods: We first determined the efficacy of the antioxidant co-therapy of Nrf2 activation (using RTA 408) and NOX inhibition (using AEBSF) in an in vitro model of epileptiform activity, low Mg²⁺ model. Utilizing live cell imaging, we measured ROS generation in real time, mitochondrial membrane potential depolarization (Δm), and epileptiform activity induced neuronal death.

We induced SE in rats using kainic acid (KA) for in vivo experiments, and wireless electrocorticography (ECoG) telemetry devices were implanted in rats to monitor the development of spontaneous seizures. Following 2 hr of SE, rats were treated with single administration of each drug.

Results: Inhibition of NOX by AEBSF decreased Δm , the generation of ROS, and the neuronal cell death in vitro. However, a combination of both NOX inhibition and Nrf2 activation showed a greater neuroprotective effect.

Rats treated with single administration of either AEBSF or RTA 408 showed a trend to decrease in seizure frequency, which was significant only over later time points. Rats treated with both drugs showed a dramatic decrease in seizure frequency starting from 2 weeks after 1st seizure and lasted up to 12 weeks.

Interestingly, only rats treated with combination therapy showed a significant increase in the latency period.

Furthermore, 70% of animals treated with both drugs became seizure free compared to only 10% of vehicle treated animals. Following this antioxidant co-therapy, odds ratio for prevent seizure developing was 21.

Conclusions: A combination of both NOX inhibition and Nrf2 activation is the most effective mean of preventing neuronal cell death in vitro, increasing antioxidant capacity following SE, and in preventing the development of epilepsy in rats following kainic acid induced status epilepticus.

0-19

Acute reduction of the Extracellular Trans-Synaptic Protein LGI1 increases network excitability

Eleonora Lugarà, Marco Leite, Elodie Chabrol, Gabriele Lignani, Matthew C. Walker

(University College London, London, United Kingdom)

Autoantibodies against LGI1 have been detected in the serum of adult patients with limbic encephalitis, seizures and status epilepticus. It is not clear if the seizures are generated by inflammation due to the antibodies or through a direct effect of the antibodies on LGI1. LGI1 (Leucine Rich Glioma Inactivated 1) is a secreted trans-synaptic protein which interacts presynaptically with Kv1.1 potassium channels and ADAM23, a membrane-anchored protein with no catalytic effect. Postsynaptically, LGI1 influences AMPA and NMDA receptors through a direct link with the ADAM22 adhesion protein. Mutations in the gene encoding LGI1 lead to temporal lobe epilepsy in humans and animal models.

We, therefore, asked if an acute reduction in LGI1 was sufficient to increase network excitability and promote seizure activity.

For this purpose, we chose and validated a silencing RNA (shRNA) against LGI1. In neuronal cultures and in ex vivo granule cells, shRNA against LGI1 increased neuronal firing. Local field potential (LFP) of ex vivo slices after injection of shRNA-LGI1 in the hippocampus, revealed an increase in the facilitation of mossy fibers to CA3 pyramidal cell neurotransmission. Application of Kv1 family blocker, alpha-dendrotoxin, occluded the increased facilitation in shRNA-LGI1 injected mice.

These results indicate that an acute reduction in LGI1 is sufficient to increase neuronal network excitability. Specifically, acutely decreasing LGI1 protein affects synaptic excitability and short-term plasticity in DG-CA3 hippocampal circuitry.

0-20

Argonaute-2 sequencing of rodent status epilepticus models identifies multiple microRNA targets for seizure suppression

Gareth Morris^{1,2,3}, Morten Venø⁴, Cristina Reschke^{1,2}, Sebastian Bauer^{5,6}, Yan Yan⁴, Tobias Engel^{1,2}, R Jereon Pasterkamp⁷, Jochen HM Prehn^{1,2}, Stephanie Schorge³, Felix Rosenow^{5,6}, Jorgen Kjems⁴, David C Henshall^{1,2}

¹FutureNeuro Research Centre, Dublin, Ireland, ²Royal College of Surgeons in Ireland, Dublin, Ireland, ³University College London, London, United Kingdom, ⁴Aarhus University, Aarhus, Denmark, ⁵Philipps University Marburg, Marburg, Germany, ⁶Goethe University Frankfurt, Frankfurt am Main, Germany, ⁷University Medical Center Utrecht, Utrecht, Netherlands

Background: MicroRNAs are short noncoding RNAs that shape the gene expression landscape, including during the pathogenesis of temporal lobe epilepsy. In vivo deployment of oligonucleotide inhibitors, termed antagomirs, has been successful in demonstrating functional roles for several microRNAs in epilepsy models. It is unknown, however, what portion of brain-expressed microRNAs are functionally engaged or whether additional microRNAs may be targets for seizure control.

Methods: Here we sequenced Argonaute 2-loaded microRNAs in the hippocampus from three different animal models, in two species and across multiple time-points, to identify unique and shared functional microRNA changes in experimental status epilepticus. We used this to rationally inform target microRNAs for seizure suppression and tested them using antisense oligonucleotides (antagomirs) in the mouse intra-amygdala kainate model. Finally, we used electrophysiological techniques to probe the mechanistic effects of these antagomirs in naïve rodent brain.

Results: We identified over 400 Argonaute 2-loaded microRNAs in each model and found levels of almost half changed in epilepsy. We selected microRNAs that were commonly upregulated in all three animal models and performed a systematic antagomir screen which identified anti-seizure phenotypes upon inhibition of miR-10a-5p, miR-21-5p and miR-142-5p. We assessed effects of these antagomirs on network, synaptic and biophysical properties of rodent hippocampi and identified mechanisms using a target capture sequencing assay.

Conclusions: Together, these studies provide a comprehensive cataloguing of the functional microRNA in the hippocampus and a pipeline of new targets for

seizure control in experimental epilepsy. Antagomir based therapies represent a highly promising new disease-modifying therapy for epilepsy, which can suppress seizures with seemingly limited off-target effects.

O-21

Glio-neuronal imbalance in a stem cell-derived model of Tuberous Sclerosis Complex

Paula Rocktaeschel², Arjune Sen², Zameel Cader¹

¹University Of Oxford, Nuffield Department of Clinical Neuroscience, Oxford, United Kingdom, ²Oxford Epilepsy Research Group, University of Oxford, Oxford, United Kingdom

Background: Tuberous sclerosis complex (TSC) is caused by mutations in either the TSC1 or TSC2 gene and is characterised by multiple benign tumours, including so-called cortical tubers in the brain. These tubers are characterised by a disturbed laminar organisation as well as a disrupted neuro-glial composition. The glial overload is suggested to be involved in the generation of seizures which are a severe symptom in 80 % of TSC patients. However, neither the underlying causes for the glio-neuronal imbalance nor for the generation of epileptic activity are understood so far. Here, we present a stem cell-derived model of TSC to investigate the influence of environmental factors on glio-neuronal development and seizure generation in vitro.

Methods: We create an in vitro model of TSC through cortical neural differentiation of TSC2 knockout human embryonic stem cells (hES). We investigate the influence of environmental factors such as starvation and inflammation on neurodevelopment and glio-neuronal composition in vitro by using various cell-based assays such as flow cytometry and immunostainings. Furthermore, we examine potential causes for the disrupted glio-neuronal composition focusing on mTOR hyperactivation, cell cycle progression and selective neuronal vulnerability. Moreover, we specifically differentiate astrocytes from TSC2 KO hES to investigate glial function in an epilepsy context.

Results: TSC2 wildtype (WT) and KO hES produced the same proportions of neurons and astrocytes after 100 days of differentiation under normal conditions. However, starvation dramatically decreased the neuronal population and, in turn, increased the glial population suggesting that environmental metabolic factors could play an important role in the disturbed cortical development in TSC. In addition, we found increased proliferation in TSC2 KO neuronal and glial cultures as well as disrupted

mTOR-dependent cell cycle progression in TSC2 KO NSC. Furthermore, preliminary results on glial function show altered glutamate uptake which might support the generation of epileptiform networks in vitro.

Conclusion: Our observations begin to illuminate the link between the TSC2/mTOR pathway and neural development in TSC and thereby, provide a starting point for further investigations of the impact of the neuro-glial composition and glial functioning on seizure generation in TSC.

O-22

Efficacy of Intranasal Allopregnanolone in a Mouse Seizure Model

Dorota Zolkowska, Michael A. Rogawski

University of California, Davis, School Of Medicine, Sacramento, United States

Intranasal delivery (IN) is a noninvasive, efficient and safe route for drug administration that may circumvent poor gastrointestinal bioavailability. The IN route is increasingly being investigated for drugs intended to treat neurological disorders because of the potential that drugs deposited into the nasal cavity may be transported directly to the brain along the olfactory and trigeminal nerves. Allopregnanolone (5 α ,3 α -P), an endogenous neurosteroid that acts as a positive allosteric modulator of synaptic and extrasynaptic GABA_A receptors, is currently under evaluation as a treatment for status epilepticus. 5 α ,3 α -P exerts antiseizure activity in various animal seizure models, including models of status epilepticus. 5 α ,3 α -P protects against seizures when administered intravenously or intramuscularly, but it is not active orally. The objective of this study was to determine if 5 α ,3 α -P has antiseizure activity when administered by the IN route. Solutions of 5 α ,3 α -P (15 mg/ml) were prepared in 40% sulfobutylether- β -cyclodextrin sodium salt in 0.9% saline. Seizures were induced in mice with pentylenetetrazol (PTZ; 80 g/kg IP). 5 α ,3 α -P solution (6 & 10 mg/kg) or vehicle was administered IN 5, 10 and 15 min prior to administration of the PTZ. Animals were observed for 30 min following PTZ. The times to onset of myoclonic body twitches and clonic and tonic seizures were recorded. 5 α ,3 α -P was considered to have antiseizure activity if it delayed the onset of seizure signs in comparison with the time of their occurrence in vehicle-treated animals.

5 α ,3 α -P 6 mg/kg administered IN delayed the time to onset of all seizure signs with a pronounced effect on tonic hindlimb extension. At 10 mg/kg in addition to a delay in seizure signs, some animals were protected from tonic

hindlimb extension and mortality. Delay in seizure signs was evidenced when 5 α ,3 α -P was administered 5 min before PTZ but at 15 min it was less active, indicating a short acting effect.

Our results for the first time demonstrate that 5 α ,3 α -P solubilized with a cyclodextrin excipient exhibits antiseizure activity when administered into the nose. In the model test system we used, 5 α ,3 α -P acted rapidly to delay seizure onset and improve survival. Delivery by the IN route may allow 5 α ,3 α -P to be conveniently and atraumatically administered by a non-medically-trained caregiver to abort ongoing seizures.

Supported by NINDS grant #1U54NS079202.

O-23

Anticonvulsant and Neuroprotective Effects of Delayed Treatment with Midazolam in a Rodent Model of Organophosphate Exposure

Jay Spampinato, Wendy Pouliot, Bonnie Roach, Melissa Smolik, F. Edward Dudek

University Of Utah, Salt Lake City, United States

Background: Exposure to organophosphates (OP) can cause status epilepticus (SE) and irreversible neural injury. Rapid control of seizure activity is important to minimize central nervous system injury and the subsequent development of neurological and behavioral disorders. Although the standard-of-care for OP-induced SE is administration of benzodiazepines, the anticonvulsant effect of these agents has been reported to decrease as the duration of SE is prolonged. However, the effect of delayed treatment with midazolam (MDZ) on electrographically recorded seizures and subsequent neuronal death resulting from OP-induced SE has not been studied quantitatively as a function of time.

Methods: Male, Sprague Dawley rats (150-200 g) were implanted with electrodes for recording of the electroencephalogram (EEG) 1 week prior to the testing. On the day of treatment, SE was induced by administration of diisopropyl fluorophosphate (DFP). At 30, 60 or 120 min after the start of SE, rats were administered MDZ (2 mg/kg). EEG was recorded for 24 hr, at which time the rats were perfused, and the brains were sectioned and labeled with Fluoro-Jade B (FJB). Neuropathology was assessed as the number of FJB 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: At 30, 60 and 120 min after the start of SE, MDZ treatment significantly reduced both seizure power as well as EEG spike frequency for several hours. However, at all three time points, MDZ did not completely terminate electrographic SE and had no significant effect on neuronal death. However, when data for MDZ treatment were combined from all three delay times, a small but significant reduction in global neuronal death was detected when compared to vehicle treatment.

Conclusions: These data demonstrate that treatment of OP-induced SE by MDZ can reduce seizure intensity even when delayed by as much as 120 min. However, this treatment alone was insufficient to completely stop seizures and resulted in a minimal reduction in cell death, indicating the need for better treatment options that enhance neuronal survival following OP exposure.

O-24

Rapid intranasal delivery of diazepam utilizing prodrug/enzyme formulations: a promising drug delivery strategy for outpatient treatment of seizure emergencies

Davin Rautiola¹, Patricia D. Maglalang², Narsihamulu Cheryala^{3,4}, Kathryn M. Nelson^{3,4}, Gunda I. Georg^{3,4}, Jared M. Fine⁷, Aleta L. Svitak⁷, Katherine A. Faltsek⁷, Leah R. Hanson⁷, Usha Mishra², Lisa D. Coles², James C. Cloyd^{2,5}, Ronald A. Siegel^{1,6}

¹Dept of Pharmaceutics, University of Minnesota, Minneapolis, United States, ²Center for Orphan Drug Research, Minneapolis, United States, ³Institute for Therapeutics Discovery & Development, Minneapolis, United States, ⁴Department of Medicinal Chemistry, University of Minnesota, Minneapolis, United States, ⁵Department of Experimental and Clinical Pharmacology, University of Minnesota, Minneapolis, United States, ⁶Department of Biomedical Engineering, University of Minnesota, Minneapolis, United States, ⁷Neuroscience Research, Health Partners Institute, Minneapolis, United States

Background: Diazepam is effective in interrupting status epilepticus and halting acute repetitive seizures. It is imperative to achieve a therapeutic concentration of diazepam as quickly as possible, because 1) seizures become increasingly difficult to control when treatment is delayed, so a short window of opportunity exists when rescue therapy with benzodiazepines, such as diazepam, is maximally effective; and 2) the risk of life-threatening complications and permanent neuronal damage increases with prolonged seizure activity. Substantial effort and

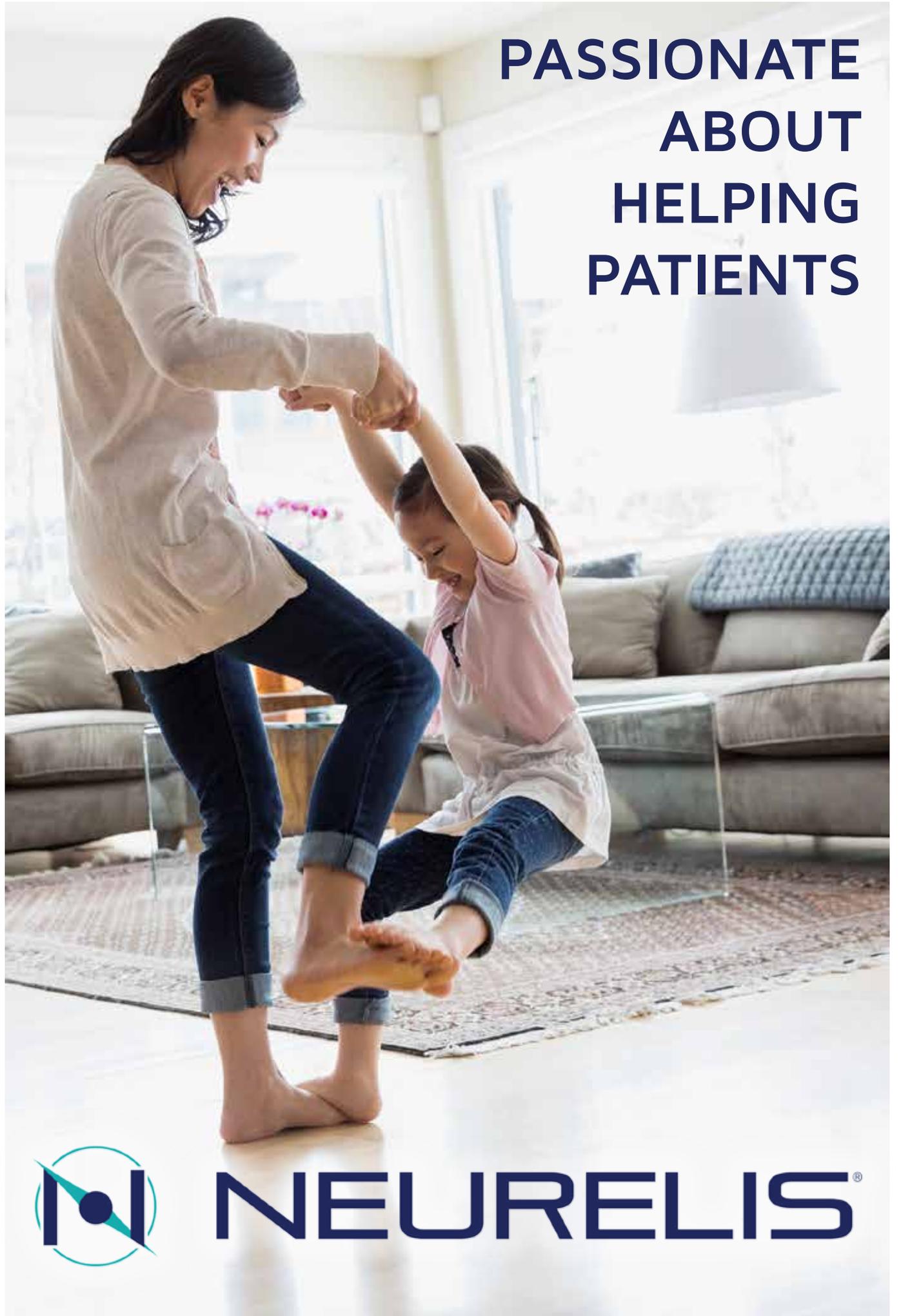
resources have been dedicated to developing a safe, rapid-acting diazepam nasal spray that can be administered in emergency situations or prophylactically by patients who experience auras. However, formulating an aqueous solution of diazepam for a nasal spray device has been challenging because the drug has very low solubility. This solubility issue can be circumvented by co-administering a hydrophilic prodrug of diazepam with a converting enzyme. Besides addressing solubility, this strategy leads to an increase in the chemical activity gradient that drives drug absorption.

Methods: A pharmacokinetic study in rats was performed. Single doses of a hydrophilic diazepam prodrug, avizafone (equivalent to diazepam at 0.500, 1.00, and 1.50 mg/kg), and a converting enzyme, human aminopeptidase B, were administered intranasally. Resulting diazepam concentrations were measured in plasma samples and in whole brain homogenates at time points ranging from 2

to 90 minutes.

Results: Both diazepam and a transient open ring intermediate were readily absorbed through the nasal mucosa, with first order absorption rate constants $0.122 \pm 0.022 \text{ min}^{-1}$ for the intermediate and $0.0689 \pm 0.0080 \text{ min}^{-1}$ for diazepam. For the low, medium, and high dose levels respectively, bioavailabilities were 77.8 ± 6.0 , 112 ± 10 , and 114 ± 7 %; maximum plasma concentrations were 71.5 ± 9.3 , 388 ± 31 , and $355 \pm 187 \text{ ng/mL}$; and times to peak plasma concentration were 5, 8, and 5 min.

Conclusions: Our results demonstrate that practically insoluble diazepam can be delivered intranasally with rapid and complete absorption by co-administering avizafone with aminopeptidase B. Therapy based on this aqueous drug formulation approach is expected to result in swift rescue from seizure emergencies, with an excellent safety profile.



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P01

Novel Use of the 'Photosensitivity Model of Epilepsy' to Identify the Rapidity of Anti-Epileptic Drug (AED) CNS Penetration: Implications for Future Choice in iv Treatment of Status Epilepticus (SE)

Ronald Reed¹, William Rosenfeld², Susan Lippmann², Dorothee Kasteleijn Nilst Trenite^{3,4}

¹West Virginia University, Morgantown, United States, ²Comprehensive Epilepsy Center, St. Louis, United States, ³Sapienza University, Rome, Italy, ⁴Utrecht University, Utrecht, Netherlands

Background: The overall 40-70% efficacy rate for status epilepticus (SE) treatment by AEDs is not optimal; time required to abort seizures is key. The conventional human Phase-IIa "Photosensitivity Model in Epilepsy" has been successfully utilized to identify efficacy of single oral doses of potential new AEDs, including Levetiracetam-(LEV) and brivaracetam-(BRV); both suppressed EEG photosensitivity response at >1h. In order to assess differences in time to effect of intravenous neuroactive AEDs, the Model's procedure needs to be conducted every few minutes. The conventional 'Model' involves simultaneous, intermittent (regular, hourly intervals x12hr) photic-induced EEG+blood sampling for concurrent AED concentration. EEG measurements are time-intensive, requiring 7-10min of operational activity (3-eye conditions at separate flash frequencies [2-60 Hz]) per photic-stimulation-result. 'The Model' methodology has not yet been applied to i.v. AEDs, where EEG effect is anticipated in <30min.

Methods: The 'Model' needed to become more time efficient; we adapted it:

- i. by studying AED-produced change in each volunteer-patient's EEG upper limit/threshold only (Kasteleijn-Nilst Trenite DG, Reed RC. *Epilepsy Curr* 2013; 13 (Suppl 1).
- i. by limiting 3 eye conditions to a "best one" (via screening photosensitivity-data);
- ii. by eliminating some high Hz, and all lower, measurements;

With these adaptations, we devised a prospective, randomized, crossover, controlled iv 2h study using frequent measurements of the evoked Photo-paroxysmal EEG Response (PPR) as a pharmacodynamic(PD) efficacy endpoint. We conducted an intra-patient comparison of three PD metrics (time to effect-time to peak effect-magnitude of effect), in adult photosensitive epilepsy patients, time 0-2h, post-15-min zero-order infusion LEV 1500 mg versus equipotent BRV 100 mg, on two separate occasions, in random, crossover, double-blind fashion (n=8 patients).

Results: We adapted 'The Model' such to be able to elicit data to compare the rapidity of effect of two similar AEDs given intravenously. The adaptation of 'The Model' has worked in the first patients being investigated (comparative AED EEG data generated).

Conclusion: Adaptation of the standard "Photosensitivity Model" should allow the determination of differences (if it exists) in time to CNS entry (effect) of i.v. infusion of two nearly identical AEDs. Data obtained in such a manner could help SE treatment algorithms.

P02

Possible epigenetic regulatory effect of dysregulated circular RNAs in epilepsy

Woo-jin Lee, Hang-Sang Lee, Hye-Rim Shin, Eun-Young Kim¹, Hyoshin Son, Yong-Won Shin, Hyeyoun Chang, Soon-Tae Lee, Kyung-Il Park, Kon Chu, Sang Kun Lee

Seoul National University Hospital, Seoul, South Korea

Background: Circular RNAs (circRNAs) involve in the epigenetic regulation and its major mechanism is the sequestration of the target micro RNAs (miRNAs). We hypothesized that circRNAs might be related with the pathophysiology of chronic epilepsy and evaluated the altered circRNA expressions and their possible regulatory effects on their target miRNAs and mRNAs in a mouse epilepsy model.

Methods: The circRNA expression profile in the hippocampus of the pilocarpine mice was analyzed and compared with control. The correlation between the expression of miRNA binding sites (miRNA response elements, MRE) in the dysregulated circRNAs and the expression of their target miRNAs was evaluated. As miRNAs also inhibit their target mRNAs, circRNA-miRNA-mRNA regulatory network, comprised of dysregulated RNAs that targets one another were searched. For the identified networks, bioinformatics analyses were performed.

Result: Forty-three circRNAs were dysregulated in the hippocampus (up-regulated, 26; down-regulated, 17). The change in the expression of MRE in those circRNAs negatively correlated with the change in the relevant target miRNA expression ($r=-0.461$, $P<0.001$), supporting that circRNAs inhibit their target miRNA. 333 dysregulated circRNA-miRNA-mRNA networks were identified. Gene ontology and pathway analyses demonstrated that the up-regulated mRNAs in those networks were closely related to the major processes in epilepsy. Among them, STRING analysis identified 37 key mRNAs with abundant

(≥4) interactions with other dysregulated target mRNAs. The dysregulation of the circRNAs which had multiple interactions with key mRNAs were validated by PCR.

Conclusion: Dysregulated circRNAs might have a pathophysiologic role in chronic epilepsy by regulating multiple disease relevant mRNAs via circRNA–miRNA–mRNA interactions.

P03

Two Russian cases of malignant migrating partial seizures of infancy due to KCNT1 mutations

Alexey Kholin¹, Inessa Fedonyuk², Anna Antonets³, Ilya Komar'kov³, Elena Il'ina², Nikolay Zavadenko¹

¹Department of Child Neurology, Neurosurgery and Medical Genetic, Pirogov Russian National Research Medical University, Moscow, Russian Federation, ²Department of Psychoneurology N2, Russian Children Clinical Hospital, Moscow, Russian Federation, ³Center of Medical Genetics "Genomed", Moscow, Russian Federation

Background: Malignant migrating partial seizures of infancy (MMPSI) or Coppola-Dulac syndrome is severe form of epileptic encephalopathy developing migrating multifocal status epileptic of polymorphic seizure types. This epileptic syndrome has heterogenic etiology including autosomal dominant mutations in gene KCNT1 encodes a sodium-activated potassium channel. OMIM genetic classification for this type of MMPSI is early infantile epileptic encephalopathy, type 14 (EIEE14; 614959).

Methods: DNA sequencing - panel "Hereditary epilepsy" (Next Generation Sequencing on platform IlluminaNextSeq 500, USA) was done for two Russian girls with MMPSI. Diagnose was verified by clinical observation with dynamical video-EEG monitoring investigation ("Encephalan-Video" RM-19/26 "Medicom MTD", Russia). 1,5 TI MRI (Siemens, Germany) revealed no dysplastic changes.

Results: In two unrelated Russian girls with MMPSI - M.V., 3 years and 3 month old and T.V., 9 month old were newly identified de novo mutations in KCNT1 gene. Girl T.V. has renowned mutation in chromosome 9: 138651532G>A with amino acid substitution Gly288Ser (OMIM: 608167.0010). The girl M.V. has previously not described mutation in 12 exome KCNT1 gene (chr9:138656907C>T, rs752514808) with amino acid substitution Arg356Trp. Mutations were confirmed by Sanger sequencing. Girl M.V. had seizure onset at the age of 4 month with seizures of behavior arrest and tonic versive. Girl T.V. developed seizures at 4,5 months in the manner of

behavior arrest and ophthalmo-clonic seizures with hyperemia of face. Both the girls had further developing typical clinical and EEG characteristics of MMPSI. T.V. was resistant to valproates and hormone therapy, aggravation on levetiracetam, oxcarbazepine and barbiturate (pagluferalum-1), but with positive effect to combination of topiramate and benzodiazepine (nitrazepamum). M.V. demonstrated resistance to valproates, lamotrigine, topiramate, levetiracetam, oxcarbazepine, ethosuximide, zonisamide, benzodiazepines and hormone therapy, with weakly positive effect to barbiturate (pagluferalum-1) and rufinamide treatment was started.

Conclusions: KCNT1 is a major disease-associated gene for the MMPSI phenotype. All the children with pharmaco-resistant epileptic encephalopathy need complex investigations including dynamic video-EEG monitoring, high quality neuroimaging, but also genetic investigation. Next Generation Sequencing (NGS) methodics - panel "Hereditary epilepsy" and whole exome sequencing are more preferable.

P04

Characterisation of an infantile rat model of de novo status epilepticus: long-term outcomes

Geatano Terrone^{1,2}, Rossella Di Sapia¹, Alessia Salamone¹, Ilaria Craparotta³, Nosaibeh R. Zaniani¹, Daniele Tolomeo¹, Edoardo Micotti¹, Sergio Marchini³, Teresa Ravizza¹, Annamaria Vezzani¹

¹Departments of Neuroscience, Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Milano, Italy, ²Department of Translational Medicine, Federico II University, Naples, Italy, ³Departments of Oncology, Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Milano, Italy

Background: Paediatric status epilepticus (SE) may result from acquired, metabolic, immune, genetic or unknown causes. We characterized an infantile rat model of de novo SE to study the pathologic sequelae ignited by unremitting seizures in the immature brain that include atrophy, cognitive deficits and epilepsy.

Methods: SE was induced by unilateral intra-amygdala injection of 2 µg kainic acid (KA) in cortical electrode-implanted postnatal day (P)13 male rat pups. Controls were injected with saline. Astrocytes and microglia activation and Fluoro-Jade-positive degenerating neurons were analyzed by immunohistochemistry and confocal microscopy; neuroinflammation and oxidative stress markers were measured by RTqPCR. Different cohorts

of SE-exposed P13 rats were longitudinally video-EEG monitored, exposed to the Morris Water Maze to test learning and memory, and to T2-weighted MRI sequence to determine brain atrophy.

Results: EEG monitored convulsive SE was defined by the appearance of continuous spikes with a frequency >1.0 Hz and an amplitude at least 2.5-fold higher than the standard deviation of the baseline tracing. SE occurred 31.0 ± 2.3 min after KA injection and lasted for 3.5 ± 0.5 h (mean \pm SEM, $n=9$). Epileptiform events of higher amplitude were recorded in the cortex ipsilateral to injected amygdala vs the contralateral homotypic area. During SE pups displayed masticatory movements, salivation, forelimb myoclonus, loss of posture. Glia activation, induction of the iktogenic cytokines IL-1 β and TNF- α and HMGB1, oxidative stress markers were measured in rats ($n=6-7$ rats each group) from 2 h to 1 week post-SE. Degenerating neurons were detected in cortex, hippocampus, amygdala, striatum and reticular thalamic nucleus. Spontaneous recurrent seizures (3-5/week) developed around 1 month after SE in about 60% of rats as assessed by video-EEG recording for at least 5 months ($n=19$). SE was similar in onset, severity and duration in all animals. MRI showed progressive atrophy in cortical and subcortical regions starting before epilepsy onset. Rats displayed cognitive impairment after epilepsy onset denoting an encephalopathic effect of spontaneous seizures.

Conclusions: This infantile SE rat model can be exploited for mechanistic studies, to test novel drugs and for developing biomarkers of disease onset and progression.

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P05

Paediatric Status Epilepticus: identification of prognostic factors using the new ILAE classification

Nicola Pietrafusa, Marina Trivisano, Luca De Palma, Marcello Bellusci, Lucia Fusco, Simona Cappelletti, Federico Vigeveno, Nicola Specchio

"Bambino Gesù" Children's Hospital, Rome, Italy

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 ILAE.

Methods: 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 semiologies ($p < 0.05$) 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.

P06

Some epidemiological aspects of status epilepticus in the female epilepsy

Svetlana Kravtsova, Michael Aleksandrov, Galina Odintsova, Alexey Ulitin

Russian A.L. Polenov Neurosurgical Institute - A Branch of The Almazov National Medical Research Centre, St. Petersburg, Russian Federation

Background: Status epilepticus (SE) is a formidable manifestation of epilepsy. The study of the clinical features of polymorphism of epilepsy from the position of predictors of status epilepticus in female epilepsy is an urgent task.

Methods: The study included 155 women of reproductive age (16-45 years). Inclusion criteria was a verified diagnosis

of epilepsy according to the ILAE classification (2017), based on a combination of clinical, electroneurophysiological and neuroradiological survey data. SE present in some women's history was taken into account according to the status epilepticus new ILAE classification of SE (2015).

Results: By type of therapy, patients with epilepsy were divided into 3 groups. The first group consisted of patients receiving monotherapy AED (68 - 44%), the second group included women who are on polytherapy AEDs (67 - 43%). In the third group patients did not receive AEDs in the last six months (20 - 13%). The average age was 25.6 ± 5.5 years and accounted for the optimal reproductive period. Tonic-clonic status epilepticus was found in 6 patients in history, which amounted to 3.9%. Of the patients of the first group - SE in history there was only one case, in the second group - in 5 women, in patients of the third group of status epilepticus in the history was not. One of the predictors of the possible development of SE is the duration of the disease. In our observations in patients of the first group, the average duration of epilepsy was 10 years, in the second group 15 years, in third group 3-5 years. According to our observations, in 17%, provocation of SE was caused by changes in the concentration of AEDs and hormonal status during pregnancy.

Conclusions: The frequency of SE in women of reproductive age is higher with resistant forms of the disease. A special feature in female epilepsy is the provocation of SE by specific hormonally-induced changes. Of particular danger is the status epilepticus during pregnancy and childbirth. The reported study was funded by the Russian Foundation for Basic Research (RFBR), research project N^o 18-013-00222.

P07

Status epilepticus; Experience in our intensive care unit since 2014

Luisa M Charco-Roca¹, Alberto Grande-Martín², Jose M Jimenez-Vizueté³, Ramón Peyró-García⁴, Pedro M Canales-Lara⁵, Carlos Martínez-Villar⁵, Llanos Sánchez-López⁵

¹Area Specialist Practitioner, Anaesthesiology and Intensive Care Service, General University Hospital Of Albacete, Albacete, Spain, ²Area Specialist Practitioner, Clinical Neurophysiology, General University Hospital Of Albacete, Albacete, Spain, ³Section Chief, Anaesthesiology and Intensive Care Service, General University Hospital Of Albacete, Albacete, Spain, ⁴Service Chief, Anaesthesiology and Intensive Care Service, General University Hospital Of Albacete, Albacete, Spain, ⁵Hospital Resident, Anaesthesiology and Intensive Care Service, General

University Hospital Of Albacete, Albacete, Spain

Background: Status epilepticus (SE) is a condition secondary to a failure of the control mechanisms for seizure termination or initiation, which leads to abnormally prolonged seizures. It is a condition that can have long-term consequences including neuronal death, neuronal injury, and alteration of neuronal networks. In Europe, the incidence of SE is 9,0 – 27,2 patients per year. Different studies point to a mortality rate between 11 and 37 %, with this rate being higher in refractory SE. As such, SE is a neurological emergency with considerable mortality and morbidity rates.

Methods: We analyzed 40 cases of SE admitted in our intensive care unit (ICU) between 2014 and 2018.

Results: 62,5% of our cases were diagnosed as non-convulsive status epilepticus (NCSE) in the setting of arreactive coma and the remaining 37,5% were diagnosed after seizures. The most common cause of SE was traumatic brain injury (35%). Another cause was drugs, ischemic strokes, intracranial masses or inadequate epileptic treatment. 4/40 (10%) of NCSE was refractory and 24/40 (60%) was superrefractory. The global mortality rate was measured to be 35%, which increased to 37,5% for patients in super refractory non convulsive status. The average stay in the Intensive Care Unit was 30 days. The most frequent complication (affecting 50% of the patients) was nosocomial pneumonia (pneumonia associated with mechanical ventilation).

Conclusions: SE is a neurologic emergency with high mortality, especially NCSE. For the diagnosis of SE, a high degree of clinical suspicions is necessary, as well as an EEG to confirm the diagnosis. The treatment of epileptic crisis and status epilepticus should be performed in an ICU with cerebral electrical activity monitoring. A multidisciplinary team with neurologist, intensivist and electrophysiologist is required to diagnosis and treat SE.

P08

Evaluation of our Psychogenic non-epileptic seizure status

İbrahim Bora, Aylin Bican Demir

University, Bursa, Turkey

Psychogenic non-epileptic seizures are the most common paroxysmal medical condition misdiagnosed as epilepsy. They significantly affect quality of life and functional status of patients.

Episodes of recurrent, prolonged PNES also called "non-epileptic psychogenic status" and defined as episodes lasting more than 30 minutes and occur in one-third of patients with PNES. Prolonged PNES can mimic Status Epilepticus (SE).

Patients with prolonged PNES are incorrectly evaluated as SE by inexperienced physicians and these patients are intubated and sent to epilepsy centers.

This study included twelve patients with PNES who were admitted to the emergency service for more than 30 minutes or patients with prolonged PNES who were admitted to the emergency room in the intubated state with real SE in mind.

Then, all patients were diagnosed with PNES by monitoring in VEM unit. While 3 patients had mixed seizures (both real and psychogenic) 9 patients had only PNES or PNES status during VEM.

Psychiatric consultation and psychometric tests were applied to all patients.

Patients with psychogenic status are incorrectly admitted to the intensive care unit and undergone unnecessary parenteral antiepileptic drug treatment.

As a result, PNES status and actual SE separation are not easy. Diagnosis can only be made by monitoring the patients in VEM unit. The increase in experienced neurologists related to the subject will facilitate the diagnosis.

P09

Development of Status Epilepticus Fast Track

Sineenard Pranboon^{1,3}, Somsak Tiamkao^{2,3}

¹Nursing Division, Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand, ²Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand, ³Integrated Epilepsy Research Group, KhonKaen University, Khon Kaen, Thailand

Background: status epilepticus (SE) is a neurological emergency and life-threatening condition leading to high morbidity and mortality rate that requires early diagnosis and prompt medical management. The objective of this study to analysed the system of care of SE patients including development and implement of SE fast track

Materials and Methods: We reviewed data of adult SE patients admitted in the year 2017 in Srinagarind Hospital. SE patients were diagnosed and searched based on ICD 10 (G41) from the database. We performed for three phase follow by 1) Situation analysis system of care 2) Development the guideline of SE fast track 3) Implement the guideline of SE fast track

Results: There were 35 case SE patients. The average age was 59.8 years and 18 patients were males (51.4%), 17 patient were female (48.6%). Type of SE ; generalized tonic- clonic status epilepticus (GCSE) 15 case (42.8%), GCSE + non convulsive status epilepticus (NCSE) 12 case (34.3%) and NCSE 8 case (22.9%). Situation analysis system of care of status epilepticus patients, we found that delayed of treatment cause by delayed diagnosis and delayed received intravenous antiepileptic drugs (AEDs); average time to diagnosis = 155.7 min and average time to treatment = 41.74 min. Development the guideline of SE fast track follow by 1) Developing the system of consultation by consult neurologist immediately 2) Developing the system of intravenous AEDs SE Box consist of 4 drugs; Phenytoin, Phenobarbital, Sodium valproate, and Levetiracetam encloses with all drug information sheets to reduce the waiting time and improve effectiveness of SE treatment. 3) Early diagnosis by perform electroencephalography (EEG) available all time. Implement the guideline of status epilepticus fast track in area of intensive critical care, medicine department and emergency department for improve outcome of treatment.

Conclusions: Development of SE fast track will reduce time to diagnosis and time to treatment leading to decrease mortality rate and morbidity in SE patient.

P10

Structural findings in patients with pharmacoresistant temporal epilepsy after anterior temporal lobectomy with a history of status epilepticus

MD Valery Bersnev¹, PhD Svetlana Kravtsova¹, PhD Tamara Stepanova¹, MD Vugar Kasumov¹, MD Olga Gaykova², PhD Galina Odintsova¹, PhD Natalia Yaremenko¹, PhD Ksenia Zagorodnikova², Dr Daria Sitovskaya¹, MD Aleksey Ulitin¹, MD Yulia Zabrodskaya¹

¹Russian A.I. Polenov Neurosurgical Institute - A Branch Of The Almazov National Medical Research Centre, St. Petersburg, Russian Federation, ²Almazov National Medical Research Centre, St. Petersburg, Russian Federation

Background: Status epilepticus (SE) is the most severe complication in patients with pharmacoresistant epilepsy. The study of neurophysiological and structural-morphological changes of the brain in patients operated on for temporal epilepsy and with epileptic status in history is an urgent task.

Methods: All patients had a confirmed diagnosis of epilepsy in accordance with the classification of the International Antiepileptic League (ILAE, 2017), based on a combination of clinical, electroneurophysiological and neuroradiological studies. The presence of SE in the history of some patients was taken into account in accordance with the new classification of the epileptic status ILAE 2015.

Results: In total, 63 patients with pharmacoresistant temporal epilepsy aged 19 to 52 years were examined and operated on. Tonic-clonic status epilepticus was found in 8 patients in history.

In all cases, histological examination of tissues removed during the operation was performed. In some cases, electron microscopy was also performed.

Among 8 patients with a history of tonic-clonic status epilepticus, various histological changes in the removed brain tissue were found. Focal cortical dysplasia (FCD) detected in 2 patients. In 3 cases, mesial temporal sclerosis (MTS) occurred.

Changes in glia in epileptogenesis foci deserved special attention. All 8 patients with a history of status epilepticus had a very mild astrocytic reaction with the presence of demyelination foci in the cortex and subcortex.

In contrast, in patients without a history of status epilepticus, glial reactions were very pronounced.

According to our data, pronounced gliosis of the white matter of the temporal lobe was characteristic of those patients in whom epilepsy proceeded along a lighter clinical type, without status epilepticus and without serial seizures.

Conclusions: Based on the research we have carried out, we have put forward an innovative hypothesis: gliosis in the epileptogenesis foci is a protective, adaptive response. Gliosis in this case is not a pathological reaction, but on the contrary, it is part of sanogenesis.

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P11

Usefulness of the brain perfusion SPECT in the diagnosis of nonconvulsive status epilepticus

Sonia Jaraba Armas^{1,2}, Gabriel Reynes³, Jacint Sala¹, Jordi Pedro⁴, Misericordia Veciana⁴, Júlia Miró¹, Oriol Puig⁵, Jaume Mora⁵, Mercè Falip¹

¹Epilepsy Unit, Neurology Department, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain, ²Neurology Department, Hospital de Viladecans, Viladecans, Barcelona, Spain, ³PET Unit, Institut de Diagnòstic per la Imatge, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain, ⁴Neurophysiology Unit, Neurology Department, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain, ⁵Nuclear Medicine Department, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain

Background: The diagnosis of status epilepticus (SE) can pose a challenge. EEG patterns can be difficult to interpret, and the absence of an EEG correlate does not rule out the diagnosis of SE. In this setting, the value of neuroimaging tools to help in the diagnosis is crucial. Our aim is to evaluate the role of HMPAO-SPECT in patients with clinical suspicion of SE, and to evaluate its value in the final diagnosis of SE.

Methods: We recruited consecutive patients admitted in our center with the suspicion of SE, and selected those who underwent a HMPAO-SPECT. All patients were admitted under neurology ward, and underwent an EEG. We divided the patients in those who were finally diagnosed of SE (SE-p) and those who not (non-SE).

SPECTs were acquired in a Skylight SPECT (Philips Healthcare, Amsterdam). The injections were done during the clinical episode suspected to be a SE. All data was normalized to the SPM SPECT template. We used an external healthy normal database (McNally KA, et al. 2005) to obtain a Z-score map from each individual versus the normal database. The Z-score maximum (Z_{max}) was extracted from each region of the AAL atlas as well as the percentage of voxels with a Z-score higher than 2.0 (N(%)). A logistic regression combining the Z_{max} , N(%)

and the effect of patient age was fitted to predict the final SE diagnosis. A receiver operator characteristic curve (ROC) and the area under the curve (AUC) were obtained to evaluate the classification performance.

Results: We included 54 patients, 21 were women (38.9%), with a median age of 62.1 years old (range 25-84). 34 patients were in SE (62.9%). The Z_{max} and N(%) were significantly higher in SE-p than in non-SE patients ($p = 0.005$ and $p < 0.001$, respectively). Results from the logistic regression presented an AUC of 0.79. Comparing both SE-p and non-SE groups, a statistical trend was found in age, being the SE-p patients older than the non-SE group ($p = 0.06$). Sensitivity and specificity using the Youden index optimal cutoff value were 0.82 and 0.81, respectively.

Conclusion: HMPAO-SPECT can be useful in the diagnosis of SE.

P12

Non-convulsive status epilepticus in acute alcoholic poisoning

Ekaterina Povaliukhina¹, MD Michail Aleksandrov¹, PhD Tatyana Aleksandrova², MD Aleksey Ulitin¹

¹Almazov National Medical Research Center, Polenov Neurosurgical Research Institute (branch, Clinic), Saint-Petersburg, Russian Federation, ²Saint-Petersburg Research Institute of Emergency Care named after II. Dzhanelidze, Saint-Petersburg, Russian Federation

Background: The purpose of the study was to determine the feasibility of developing a non-convulsive status epilepticus (NCSE) in severe alcoholic coma.

Methods: 46 patients (age 19-48 years) with severe ethanol poisoning were examined. The diagnosis was confirmed by a clinico-toxicological analysis of the ethanol concentration in the blood. The study did not include patients with seizure, severe traumatic brain injuries in the anamnesis. EEG monitoring was performed from the moment of admission and until the restoration of consciousness. If the coma persisted for more than 6 hours, the study was performed after 12 hours and 24 hours. The EEG was recorded on the "Mizar-EEG-201" encephalograph (Ltd "Mizar").

Results: Of the 46 examined patients, five were diagnosed with epileptiform stigmata on the EEG. The convulsive syndrome was not observed in any case. In two cases, a relatively long unconscious state was formed in the outcome of comatose period. In one of these patients, the

state of impaired consciousness lasted 76 hours, in the other case 48 hours. When EEG was registered in a clear consciousness, epileptiform activity was not observed in these patients.

Conclusions: In severe acute ethanol poisoning, the formation of a long-term state of disturbed consciousness in the outcome of a comatose period may have the formation of a stagnant determinant with hypersynchronous activity in pathogenesis. NCSE with severe ethanol poisoning is a relatively rare event compared with the clinic of other severe cerebral lesions (severe craniocerebral trauma, disorder of cerebral circulation).

P13

Absence status epilepticus in the postictal phase of a generalized tonic-clonic seizure as the potential final manifestation of a relapsing remitting genetic epilepsy syndrome

Anna Teleki¹, Julian Bösel², Johannes Rösche³

¹Klinik für Neurologie, Klinikum Kassel, Kassel, Germany, ²Kassel School of Medicine, University of Southampton, Southampton, United Kingdom, ³Klinik und Poliklinik für Neurologie, Universitätsmedizin Rostock, Rostock, Germany

Background: In 2012 nonconvulsive status epilepticus in the postictal phase of generalized tonic clonic seizures was characterized as being associated with periodic lateralized or generalized periodic discharges in EEG. In the classification of 2015 this category was omitted and among others the relapsing absence status in the elderly introduced.

Methods: We report the case of a 82-year-old woman who presented with recurrent absence status epilepticus in the postictal phase of generalized tonic-clonic seizures.

Results: Around 1946 the patient was diagnosed to suffer from Juvenile Absence Epilepsy and successfully treated with ethosuximide and primidone. After a miscarriage in 1968 seizures relapsed and the syndrome was now classified as Generalized Tonic-Clonic Seizures Alone. Seizure frequency increased to 4-5 per year in the early 90ies and she was advised to take valproic acid. Nevertheless, she stayed on ethosuximide 500 mg and primidone 625 mg. After all she remained seizure free from 1996 till January 2018, when under a medication of ethosuximide 250 mg and primidone 500 mg a series of generalized tonic-clonic seizures occurred followed by a nonconvulsive status epilepticus. Ethosuximide was

stopped and levetiracetam was introduced to the therapy. After another series of generalized tonic-clonic seizures levetiracetam was increased to 3000 mg. In May 2018 after another generalized tonic-clonic seizure another nonconvulsive status epilepticus occurred, which was now recognized as absence status as Relapsing Absence Status in Later Life. Valproate was introduced in the therapy and primidone was tapered off. The patient remained seizure-free for the next seven months at least.

Conclusions: In nonconvulsive status epilepticus in the elderly the diagnosis of relapsing absence status should be considered because valproate seems to be a very effective treatment in this situation. Additionally, this case shows that the features of a genetic epilepsy syndrome may change in the course of time.

P14

Absence status epilepticus – a case series

Magdalena Bosak

Jagiellonian University Medical College, Kraków, Poland

Background: Absence status epilepticus (ASE) is a type of generalized non-convulsive status epilepticus in which continuous or almost continuous generalized spike-wave or polyspike-wave discharges are associated with a varying grade of consciousness impairment and at times with other clinical manifestations such as automatisms or subtle myoclonic, tonic, atonic, or autonomic phenomena. ASE can occur in all genetic generalized epilepsies (GGEs) with absence seizures, above all in juvenile absence epilepsy (JAE). The aim of the study was to present electroencephalographic (EEG) and clinical correlates of 8 cases of ASE.

Methods: EEG and clinical data of patients with ASE were prospectively registered.

Results: All patients (6 women and 2 men) suffered from GGEs; 6 had JAE, 2 had juvenile myoclonic epilepsy. The mean age at onset of epilepsy was 14 years (range 11-19) and the mean age at time of presentation was 41 years (range 28-72). ASE preceded or followed a tonic-clonic seizure in 4 patients. In one patient ASE occurred before the diagnosis of JAE was made, in other cases ASE was provoked. Triggering factors were as follows: antiepileptic drugs (AEDs) withdrawal/tapering in 3, treatment with inappropriate AEDs in 3, infection treated with antibiotics in 1 patient. EEG showed continuous or almost continuous generalized polyspike-wave discharges in 6 patients and bilateral sharp waves/ sharp and slow wave discharges in

2 patients treated with contraindicated drugs (gabapentin, tiagabine, carbamazepine) (figures 1-6). All cases of ASE were treated with iv diazepam or/and valproate with good outcome.

Conclusions: Absence status epilepticus is a rare form of nonconvulsive status epilepticus, in most cases provoked by withdrawal of medication or inappropriate medication. EEG is indispensable in diagnosis of ASE. ASE is usually easily treatable condition.

P15

Lateralized Periodic Discharges (LPDs) as ictal manifestation of Aphasic Status Epilepticus

Fedele Dono¹, Catello Vollono², Claudia Carrarini¹, Mirella Russo¹, Camilla Ferrante¹, Marco Onofri¹, Francesca Anzellotti

¹University G. D'annunzio, "SS Annunziata" Hospital, Chieti, Italy, ²Catholic University of the Sacred Heart, Rome, Italy

Background: Language disturbances can be usually found in various pathological acute pictures involving the dominant frontal and temporal lobes. Prolonged aphasia as the only manifestation of focal status epilepticus is rarely described and only a few cases have been documented. Several EEG patterns have been associated with Aphasic Status Epilepticus (ASE) including Lateralized Periodic Discharges (LPDs). LPDs pattern is usually correlated with structural lesions of cortical or subcortical areas due to some pathological conditions such as acute stroke, brain tumours, infections, traumas and metabolic diseases. The origin of LPDs is a controversial issue and only a few existing neurophysiological hypotheses address causes and circumstances of LPDs onset and if they represent an ictal or inter-ictal pattern.

Methods: We report two cases of ASE associated with LPDs. Aphasic Status Epilepticus was defined according to Rosenbaum's criteria modified by Grimes & Guberman. All these patients underwent a 21 derivations EEG recording according to the 10-20 international system, 3T Magnetic Resonance Imaging (MRI) of the brain and were tested with Aphasia Rapid Test (ART) to better define aphasia's severity. In addition, a review of the past literature was performed by the search terms "Aphasic Status Epilepticus" and "Lateralized Periodic Discharges" on PubMed. A total of 6 articles were available for further analysis.

Results: We stress the electro-clinical correlation between ASE and Lateralized Periodic Discharges. It has been

recently reported that the association between LPDs and seizure is more consistent in the presence of particular LPDs features with an increased seizure risk with higher periodic discharges frequency and "Plus modifier" such as superimposed fast activity. In the previous literature, LPDs have been sometimes associated with ASE but they have not always been marked as ictal pattern even though, in some cases, a clear electro-clinical correlation was described with patient's good clinical response to the anti-seizure therapy.

Conclusions: We highlight the importance of considering focal SE in the differential diagnosis of patients presenting aphasia and how LPDs can represent an ictal EEG pattern with regard to ASE.

P16

Aphasic Status Epilepticus Revisited

Sonia Jaraba Armas^{1,2}, Jacint Sala¹, Misericordia Veciana³, Jordi Pedro³, Àngels Camins⁴, Laura Rodríguez Bel⁵, Jaume Mora⁶, Cristina Gámez⁵, Mercè Falip¹

¹Epilepsy Unit, Neurology Department, Hospital Universitari de Bellvitge, L'Hospitalet De Llobregat, Barcelona, Spain, ²Neurology Department, Hospital De Viladecans, Viladecans, Barcelona, Spain, ³Neurophysiology Unit, Neurology Department, Hospital Universitari de Bellvitge, L'Hospitalet De Llobregat, Barcelona, Spain, ⁴Radiology Department, Institut de Diagnòstic per la Imatge (IDI), Centre Bellvitge, Hospital Universitari de Bellvitge, L'Hospitalet De Llobregat, Barcelona, Spain, ⁵PET Unit, Institut de Diagnòstic per la Imatge (IDI), Hospital Universitari de Bellvitge-IDIBELL, L'Hospitalet de Llobregat, Barcelona, Spain, ⁶Nuclear Medicine Department, Hospital Universitari de Bellvitge - IDIBELL, L'Hospitalet de Llobregat, Barcelona, Spain

Background: Prolonged aphasic status epilepticus (ASE) in patients without previous seizures and unknown cerebral lesions is rare, and in many occasions an acute stroke is suspected. Some of these patients may be thrombolised and admitted into stroke units. The aim of the study is to describe electroclinical and neuroimaging characteristics, aetiologies and outcome of patients presenting as de novo ASE.

Methods: We designed an unicentric study including consecutive patients presenting to the Neurology Service with new onset status epilepticus of unknown origin (NORSE) between 2011 to 2018. Final diagnosis was obtained after an acute phase complete work-up and considering the follow-up as an outpatient (minimum one year). Patients with ASE (considering aphasia as the

main seizure type) were selected. Aetiology and diagnostic procedures included: video-EEG monitoring, serum and CSF biochemistry, serologies and PCR for neurotropic agents, nonspecific immunological analysis and antineuronal antibodies and onconeuronal antibodies. Necropsic studies were performed in some cases. Neuroimaging studies included ictal SPECT, MRI with a protocol for status epilepticus and FDG-PET.

Results: From 35 patients with NORSE, 16 patients (43%) with ASE were selected. 13 (81%) were women, mean age 70.4 (SD14.5), mean age at ASE onset 66 (SD 15.9), 9 (56%) patients had died. TC scan, done in the first 24 hours, was normal in all patients. MRI done during the first week was normal only in 3 patients (17.5%), in 4 (25%) periictal changes were found. First available EEG was normal or showed minor abnormalities (focal slowing or generalized slowing) in 6 (40%), in 5 patients (31%) seizures were recorded and the rest showed a lateralized periodic pattern. SPECT and/or PET were available in 12 patients and showed focal hypermetabolism or hyperperfusion in 8 (66%). Final aetiologies were symptomatic epilepsy (6), toxic/metabolic (2), amyloid angetitis (2), SMART syndrome (1), infectious encephalitis (1), unknown (2), neurodegenerative disorder (1), autoimmune systemic disease (1). Only 4/16 (25%) responded to corticotherapy. No patient with limbic encephalitis debuted with ASE.

Conclusions: Aphasic status epilepticus is a severe entity in which high suspicion is needed. PET or SPECT studies may be specially helpful in diagnosing this entity.

P17

The features of status epilepticus in children with progressive myoclonus epilepsy - a single center experience

Ruzica Kravljanc, Biljana Vucetic Tadic

Institute For Mother and Child Healthcare of Serbia, Faculty of Medicine University of Belgrade, Beograd, Serbia

Background: Progressive myoclonus epilepsy (PME) is characterized by various epileptic phenotype since PME has heterogeneous etiology. The main feature of PME is neurological devastating and resistant epilepsy. The aim of the study is evaluation of status epilepticus (SE) in children with progressive myoclonus epilepsy (PME).

Methods: The retrospective study included children with PME and SE with prominent motor symptoms, treated in Institute in period from 1998 to 2018. PME was diagnosed by enzyme, genetic and/or histopathology investigations.

SE was defined as clinical seizure duration >30 min, and classified according the new classification (Trinka et al. 2015). Evaluated features were: age, type, duration, SE recurrence and response to the treatment.

Results: During the course of disease, 21 of 46 children with PME (45.65%) experienced total of 50 episodes of SE. The etiology was: neuronal-ceroid lipofuscinosis (7), Gaucher disease 2 (2), Nieman-Pick C (4), mitochondrial disorders (4), Lafora disease (2), Krabbe disease (1), KCNC1 (1). The age was 0.2-18 (mean 8.4) years. Nine patients experienced SE during the first year of disease, and in four cases, SE was the first epileptic event. All episodes had prominent motor symptoms: convulsive (25), myoclonic (13), focal including epilepsia partialis continua (12). Response to the treatment was variable, with common side effects. Most effective drug was midazolam in intravenous infusion with mean dosage of 0.35 mg/kg/h. The artificial ventilation was necessary in 7 episodes, in 4 together with circulatory support. Refractory SE was in 62% episodes, including nine SRSE. Recurrence rate was nearly 50%.

Conclusion: Children with PME frequently experience SE. Episodes are mostly convulsive, refractory to AEDs with high recurrence rate. SE appearance in later phase of disease contribute to prominent drug adverse effects. Managing SE in children with PME is challenge and requires rational approach in order to stop the seizure, and, on the other hand, to prevent side effects and worsening of general and neurological patient's condition.

P18

Refractory and super-refractory Status epilepticus-analysis of etiological factors

Cristina Munteanu^{1,2}, Stanislav Groppa^{1,2}

¹State University of Medicine and Pharmacy "Nicolae Testemițanu", Chisinau, Moldova (the Republic of),

²Institute of Emergency Medicine, Chisinau, Moldova (the Republic of)

Background: Status epilepticus (SE) can be a life-threatening condition associated with multiple complications, including death, and can progress to refractory and super-refractory SE. Treatment guidelines recently published partially addresses to the treatment of refractory and super-refractory SE.

Materials and Methods: We conducted a retrospective study of patients diagnosed as having SE- for a period of 2 years (01/01/2017-12/31/2018), according to the clinical presentation and EEG findings, also who had appropriate

instrumental diagnosis included cerebral neuroimaging with CT and MRI to identify which condition are leading to refractoriness. The following data were analysed: age, sex, SE clinical type (convulsive and non-convulsive (NCSE)), neurological presentation, EEG features, etiology according to instrumental findings, neuroimaging study (brain CT and MRI), and/or blood examinations, and response to staged applied treatment protocol.

Results: Data are presented in raw numbers, data were analysed using Excel, student's t-test, we identified 78 patients, 29 of whom were female and 49 male, with a mean age of 42.2 ± 18.4 years. Regarding clinical SE type, convulsive SE was observed in 68 patients and non-convulsive in the remaining 10/78. As regards the SE type according to age patients with convulsive SE were older than patients with NCSE. According to EEG – focal SE was in 49 cases and generalised in 29, no difference for gender, for age focal SE more characteristic for older. Lesional SE was in 52 cases, toxic-dysmetabolic in 11 patients, anoxic SE in 3 and AED non- adherence in 12 from 78 patients. The oldest patients were those with lesional SE due to posttraumatic injuries, poststroke, brain metastasis, neurosurgical interventions followed by patients with non-adherence and toxico-dysmetabolic. Also it was observed among young patients the predominance of infectious and autoimmune underlying etiology (autoimmune/ viral encephalitis), and this cases proven to be refractory to first and second- line AEDs treatment (6/10 patients with refractory SE). 22 of patients have complete SE regression after being treated with benzodiazepines, 46 needed administration of second-line drugs like- phenytoin and phenobarbital and 10 patients – 12,8 % required anesthetic drugs to control the epileptic activity (3 patients- 3,8 % developed super-refractory SE (2 case herpetic encephalitis and 1 case anoxic brain injury).

Conclusion: Predictors of refractory status epilepticus were new diagnosis of SE and nonconvulsive SE. The etiology of refractory status epilepticus appears to be similar overall to that of nonrefractory status epilepticus, but more likely associated with encephalitis (viral encephalitis, in particular) and hipoxico-anoxic brain injuries. We also can conclude that good adherence to staged treatment as well as treatment of the underlying etiology is the key to success in controlling refractory seizures.

P19

Long term follow-up of recurrent Status Epilepticus and Stroke-Like Episodes in a MELAS family

Lorenzo Muccioli, Francesca Bisulli, Lidia Di Vito, Chiara La Morgia, Laura Licchetta, Lara Alvisi, Valerio Carelli, Marco Zanello, Paolo Tinuper

IRCCS Bologna Institute of Neurological Sciences, Department of Biomedical and Neuromotor Sciences, University Of Bologna, Bologna, Italy

Background: Mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes (MELAS) is a disorder commonly caused by the A3243G/tRNA^{Leu} mutation of mitochondrial DNA (mtDNA). MELAS patients are at high risk of developing status epilepticus (SE) during stroke-like episodes (SLEs). We describe the long-term follow-up of 2 affected members of a MELAS family with recurrent focal SE associated with SLEs. SE treatment is discussed.

Method: A complete clinical work-out including clinical, biochemical, neuroradiological and EEG assessment was performed over the years in both patients.

Results: The mother developed since 33 years of age focal epilepsy (auditory and visual symptoms, hemiclonic seizures), sensorineural deafness, migraine, intestinal dysmotility, severe cognitive impairment, right homonymous hemianopsia and hemiparesis. She presented recurrent parieto-occipital SE associated with SLEs leading to death at 40 years of age.

Her son suffered photosensitive epilepsy since 17 years of age. He presented 7 episodes of occipital SE (elementary visual hallucinations and oculo-clonic seizures) associated with hemianopia, lactic acidosis and parietal-occipital SLE and refractory epilepsia partialis continua (EPC) in one occasion. SE became progressively more difficult to treat and complicated by lactic acidosis and rhabdomyolysis. During one SE propofol was used and the patient suffered multiple organ failure (propofol infusion syndrome-PRIS). Iv high-dosage midazolam was the most effective treatment of SE.

Both patients carried the mtDNA A3243G/tRNA^{Leu} mutation with a similar degree of heteroplasmy (80%).

Conclusion: We report the long term follow-up of 2 members belonging to a MELAS family with recurrent SE and SLEs. SE became refractory to treatment in both patients leading to death in the mother. Based on the occurrence of PRIS and evidence of mitochondrial toxicity, we suggest to avoid the use of propofol for SE treatment in patients with mitochondrial encephalopathy. Midazolam is well tolerated and is a therapy of choice for SE in MELAS.

P20

Tumor associated Status Epilepticus (TASE): clinical and prognostic considerations in an adult population

Giada Giovannini¹, Francesco Pasini², Niccolò Orlandi^{1,2}, Maria Cristina Cioclu^{1,2}, Jessica Rossi^{1,2}, Anna Elisabetta Vaudano¹, Laura Mirandola², Stefano Meletti^{1,2}

¹Unit of Neurology, OCSAE Hospital, AOU, Modena, Italy, ²Department of Biomedical, Metabolic and Neural Sciences; Center for Neuroscience and Neurotechnology, University of Modena and Reggio Emilia, , Italy

Background: Status Epilepticus (SE) can be the presenting symptom or a subsequent manifestation in the natural history of a cerebral neoplasm. Moreover, it is known that the risk of tumor associated SE (TASE) development is related to the tumor WHO degree with the highest degree carrying the highest risk.

Methods: We describe our case-series of TASE, focusing on glioma associated SE, collected during the time frame 2013-2018 in the OCSAE hospital of Modena, Italy.

We defined the clinical features of TASE population (20 patients) and compared TASE versus non-TASE patients (271 patients).

Results: Among the 359 consecutive patients with SE, we observed 20 patients with TASE caused by a glioma (6%): WHO diagnosis was astrocytoma (n=2), ganglioglioma (n=2), and glioblastoma multiform (GBM; n=16). 15 patients had a non-convulsive form of SE (NCSE, 75%). In 11 patients (55%) the SE determined the diagnosis of the glioma while in the others 9 was the manifestation of a clinic-radiological progression of the disease.

When compared to non-TASE, TASE patients were younger (median 69 y/o versus 76 y/o, $p < 0.005$). The response to therapy, and in particular the refractoriness to treatment was not different between the two groups ($p = 0.672$). TASE and non-TASE had the same level pre-hospital disability (measured by mRS) ($p = 0.09$), while short term (30 days) disability was significantly lower in TASE than in non-TASE ($p = 0.003$). The 30 days mortality was significantly lower in TASE group ($p = 0.04$) while the mortality at 6 and 12 months was significantly higher in the TASE group ($p = 0.001$ and $p < 0.0001$).

Conclusions: These monocentric data suggest that TASE carries the same probability of refractoriness as the other etiologies. Moreover, short term prognosis related to the SE event (either disability and mortality) is good, while it deteriorates in the long term due to the underlie condition.

P21

Post-anoxic status epilepticus: A review of our experience in the last five years

María José Hernández García, Dionisio Miguel García Alvarez, Lucas Dario Iacampo Leiva, María Dolores Villar Martínez, Gabriel Ricardo González Toledo, Carolina Hernández Javier, Francisco Carrillo Padilla

Hospital Universitario De Canarias, San Cristóbal de La Laguna, Spain

Background: Status epilepticus (SE) after cardiac arrest (CA) is associated with high mortality despite an appropriate antiepileptic treatment. The aim of our study is to determine which factors could contribute to a better prognosis in this patients, taking into account the duration of the status, EEG pattern and drugs used.

Methods: We retrospectively analysed our patients who suffered SE following CA in the last five years (2013-2018). EEG background patterns of SE, duration of SE, presence and characteristics of clinical seizures and use of antiepileptic drugs (AD) were assessed. Outcome was evaluated using the Cerebral Performance Category (CPC).

Results: We collected 34 patients admitted to the ICU after CA who presented anoxic encephalopathy. 14 patients (41.17%) developed a myoclonic status after finishing therapeutic hypothermia and onset of awakening. All were treated with a combination of AD, including valproic acid, levetiracetam, anesthetics (midazolam and propofol), occasionally phenytoin, and in two cases, ketamine and lacosamide. Five patients presented a flat encephalographic pattern while six patients showed continuous generalized paroxysmal discharges. Two patients survived (CPC: 2 and 3, respectively). Median survival of the deceased patients was 14.4 days.

Conclusions: In post-anoxic encephalopathy, SE is a frequent complication and it normally correlates with poor outcome. A continuous EEG and multimodal prognostication approach to adapt pharmacologic treatment would be necessary in order to improve the prognosis.

P22

Eucalyptus Oil Ingestion Induced Status Epilepticus: A Short Case Series

Rakesh Jadav¹, Thomas Mathew²

¹Apollo Hospitals, Bangalore, India, ²Department of Neurology, St John's Medical Collage, Bangalore, India

Introduction- Eucalyptus oil is an essential oil derived from leaf of Eucalyptus tree and is widely used as an over the counter remedy for common ailments. Here we report a small case series of 3 adults with Eucalyptus oil induced status epilepticus.

Case Presentations:

Case 1

24-year-old young man was admitted to the critical care intensive care unit of our hospital with status epilepticus of unknown cause. History was clarified from father who narrated the following incident. He (Father) had bought a bottle of eucalyptus oil at home few weeks back. As the bottle was leaking he transferred the contents from the eucalyptus bottle to another empty cough syrup bottle. His son who was apparently healthy came home in the afternoon and drank 5 ml of the liquid (Eucalyptus oil) from the cough syrup bottle as he was having some cough and cold from the morning. 5 min after drinking the syrup he had an episode of generalized tonic-clonic seizures and had multiple episodes after that. He was taken to a near by hospital for the initial treatment and was later transferred to our hospital in a critical state. In our critical care unit he was intubated and was treated for status epilepticus with lorazepam, phenytoin, levetiracetam and midazolam infusion. His CT Brain showed diffuse cerebral edema while EEG showed diffuse slowing in the delta range. He developed multiorgan dysfunction and died on the 5th day of admission.

Case 2

31-year-old man used to take few drops of eucalyptus oil mixed with water occasionally for abdominal pain for the past 3 years. He drank 2-3 tea spoon full (10-15 ml) of Eucalyptus oil for abdominal pain and had multiple episodes of generalized tonic clonic seizures, 20 minutes after the intake. He was taken to a near by hospital and was treated with intravenous antiepileptic drugs and was discharged after 5 days on Tab levetiracetam 500 mg bid. His hematological, biochemical and neurological investigations were unremarkable.

Case 3

38-year-old man was a case of post traumatic occipital lobe epilepsy and was well controlled on Tab phenytoin 300 mg per day. He had headache and cold for which he applied various balms and oils containing eucalyptus and

camphor and had multiple episodes of visual aura in the form of flashes of light with altered sensorium on going for hours suggestive of a complex partial status. His MRI brain showed occipital gliosis and EEG showed slowing from the occipital regions. He was discharged with an advice to avoid these essential oils which provoke seizures.

Discussion- Essential oils like eucalyptus have epileptogenic potential which is rarely recognized by public and physicians. These essential oils are kept in the houses in open places within the reach of everyone including toddlers as they are generally perceived as safe. Here we have described three cases of Eucalyptus oil induced status epilepticus in three young adults. The young man who expired following status epilepticus and multiorgan dysfunction had consumed it accidentally while others took as remedy for abdominal pain and upper respiratory tract infection. The epileptogenic properties of plant derived essential oils are known for centuries but public and physicians are equally ignorant of these serious complications. The essential oils which are epileptogenic are eucalyptus, camphor, thuja, sage, spike lavender and turpentine. 1 The route of exposure, the type and amount taken all may be important in causing these complications. The essential oil of eucalyptus and camphor are the ones which are commonly used and abused. These contain an aromatic monoterpene called 1,8 Cineole, which is epileptogenic compound. 1,8 Cineole has a mechanism of action similar to known anti-convulsant pentylentetrazole.² Although there have been no explicit studies outlining the mechanism by which eucalyptus oils can precipitate seizures, studies on rat models show it may be secondary to loss of tissue sodium/potassium gradient leading to increased cellular hyperexcitability.³ In cases of so called de novo status epilepticus exposure to essential oils need to be sought. Public and physicians should be made aware of the epileptogenic potential of these essential oils.

P23

Refractory non-convulsive status epilepticus with favorable outcome in a patient with Marchiafava–Bignami disease

Jin-Sun Jun¹, Hee-Jin Jo¹, Ho-Won Lee¹, Ryul Kim²

¹Kyungpook National University Chilgok Hospital, Daegu, South Korea, ²Seoul National University Hospital, Seoul, South Korea

Background: Marchiafava–Bignami disease (MBD) is a rare condition mainly associated with chronic alcoholism, which is characterized by demyelination of the corpus callosum.

MBD results in a variety of neurological symptoms including altered mentality, gait difficulty, cognitive dysfunction, and seizure. Herein, we report a patient showing a favorable outcome after refractory non-convulsive status epilepticus (NCSE) as an initial manifestation of MBD.

Methods: A case report.

Results: A 58-year-old man presented with an acute confusional state with intermittent upward eyeball deviation, which had been developed a few hours. He had a history of chronic heavy alcohol consumption. The amount of alcohol intake was about 2 bottles of Korean Soju per day. Upon neurological examination, he was disoriented and his level of consciousness fluctuated. Considering the possibility of alcohol-related symptoms, he was promptly administered intravenous (IV) thiamine 50 mg with normal saline. Routine blood tests, including tests of thiamine levels, and cerebrospinal fluid studies revealed no abnormalities. Brain magnetic resonance imaging (MRI) on admission showed hyperintense lesions involving the splenium and genu of the corpus callosum and the cerebral cortex. Electroencephalography revealed periodic rhythmic delta activities suggestive of NCSE. IV lorazepam (0.1 mg/kg) followed by IV fosphenytoin (30 mg/kg loading doses) were administered, but his clinical and electrographic seizure persisted. Seizure control was achieved on day 4, after adding levetiracetam (2000 mg/day) and lacosamide (400 mg/day). On day 7, he was oriented and was able to name objects, follow commands, and to walk with some assistance. He received IV thiamine 200 mg/day for 28 days, followed by oral thiamine 30 mg per day. Follow-up MRI at 1 month after the onset of symptoms showed persistent hyperintense lesions involving the splenium and genu of the corpus callosum, with some atrophic changes. At the 2-month follow-up, he was able to carry out many of his usual activities without assistance. He did not experience any symptom that indicated a seizure while on maintenance levetiracetam (300 mg/day) and lacosamide (400 mg/day).

Conclusion: MBD can be involved in the etiology of NCSE. Also early treatment with thiamine may be necessary for a better prognosis.

P24

Status epilepticus secondary to extensive pneumocephalus

Luisa M Charco-Roca¹, Alberto Grande-Martín², Jose M Jimenez-Vizueté³, Ramón Peyró-García⁴, Belén Cifuentes-García⁵, Juan J Pazos-Crespo⁵, Pedro M Canales-Lara⁵

¹Area Specialist Practitioner, Anaesthesiology and Intensive Care Service, General University Hospital Of Albacete, Albacete, Spain, ²Area Specialist Practitioner, Clinical Neurophysiology, General University Hospital Of Albacete, Albacete, Spain, ³Section Chief, Anaesthesiology and Intensive Care Service, General University Hospital Of Albacete, Albacete, Spain, ⁴Service Chief, Anaesthesiology and Intensive Care Service, General University Hospital Of Albacete, Albacete, Spain, ⁵Hospital Resident, Anaesthesiology and Intensive Care Service, General University Hospital Of Albacete, Albacete, Spain

Background: Pneumocephalus is a frequent pathology in the postoperative period of a craniotomy. Patients who present neurological deterioration or epileptic seizures in the postoperative period of a craniotomy require a rapid diagnosis. It is important to perform imaging and electroencephalogram tests (EEG) to diagnose surgical complications and epileptic events and initiate an early and aggressive treatment.

Methods: We report a case of status epilepticus occurring in the setting of extensive pneumocephalus after craniotomy for resection of frontal meningioma.

Results: 82-year-old who presented neurological deterioration in the immediate postoperative period of a frontal meningioma resection. Urgent computerized tomography showed a large frontal air collection (extensive pneumocephalus) with postoperative changes, without bleeding. The patient presented a complex epileptic crisis and the EEG showed status epilepticus. The patient required two anticonvulsant drugs (levetiracetam and phenytoin) and subsequent general anesthesia with midazolam and propofol. Daily EEG showed moderate-severe encephalopathy with "outbreak-suppression". After withdrawal of general anesthesia the patient presented a GCS of 3 and after 14 days the medical staff decided to limit the therapeutic effort taking into account her vital preferences and those of her family.

Conclusions: Pneumocephalus is the consequence of a traumatic violation of the dura and should be considered in all patients who present epileptic crisis after a craniotomy. Gold standard diagnostic test is CT without contrast, which can identify even small amounts of intracranial air and can

exclude other diagnoses. Epileptic status is a neurological emergency that requires immediate treatment and an early EEG must be performed.

P25

Posterior reversible encephalopathy syndrome due to chemotherapy, a case report

Luisa M Charco-Roca¹, Alberto Grande-Martín², Jose M Jimenez-Vizueté³, Ramón Peyró-García⁴, Llanos Sanchez-Lopez⁵, Juan J Pazos-Crespo⁵, Carlos Martinez-Villar⁵

¹Area Specialist Practitioner, Anaesthesiology and Intensive Care Service, General University Hospital Of Albacete, Albacete, Spain, ²Area Specialist Practitioner, Clinical Neurophysiology, General University Hospital Of Albacete, Albacete, Spain, ³Section Chief, Anaesthesiology and Intensive Care Service, General University Hospital Of Albacete, Albacete, Spain, ⁴Service Chief, Anaesthesiology and Intensive Care Service, General University Hospital Of Albacete, Albacete, Spain, ⁵Hospital Resident, Anaesthesiology and Intensive Care Service, General University Hospital Of Albacete, Albacete, Spain

Background: Posterior reversible encephalopathy syndrome (PRES) associates various neurological manifestations (headaches, seizures, altered mental status, cortical blindness, focal neurological deficits, vomiting) and transitory changes on neuroimaging consistent on cerebral edema. It has been associated with hypertension and immunosuppressive treatments, among other factors. In addition, epileptic seizures appears in the majority of cases and 20% of them show status epilepticus.

Methods: We report a case of PRES occurring in the setting of a metastatic brain tumor treated with chemotherapy and radiosurgery admitted to the intensive care unit (ICU) that develops status epilepticus.

Results: 53-year-old man with cerebellar metastases secondary to lung carcinoma treated with chemotherapy and radiosurgery the previous month. After accidental fall down the stairs he presented complex seizures. The CT showed no changes in his previous brain lesions and we started treatment with levetiracetam. Due to the persistence of the crisis, admission to the ICU was decided and valproate was added to the treatment. The electroencephalogram (EEG) showed intercritical abnormalities and moderate encephalopathy. The patient presented drowsiness, bradypsychia and right hemiparesis. After 4 days he was agitated and the EEG showed status epilepticus. Treatment with phenytoin was started. Daily EEG were performed, showing an improvement in the

registry. The lumbar puncture did not show tumor cellularity and the MRI reported findings compatible with PRES.

Conclusions: PRES is a rare disease secondary to vasogenic edema. In the majority of cases changes are localized in posterior irrigation areas of the brain. CT imaging is typically normal. The classic imaging finding of PRES in RMI are occipital subcortical vasogenic edema without signs of stroke.

The possible cause of the syndrome developed by our patient is vascular disease with endothelial damage and rupture of the blood-brain membrane secondary to chemotherapy and/or radiosurgery. The main pillars of the treatment includes blood pressure regulation, control of seizures and anti-edema therapy. The treatment of epileptic crisis and status epilepticus should be performed in an ICU with monitorization of cerebral electrical activity.

P26

Everyday nonconvulsive status epilepticus episodes in a 12-year-old girl with pharmacoresistant epilepsy of unknown etiology admitted for presurgical evaluation

Magdalena Kaczorowska-Frontczak, Dorota Domanska-Pakiela, Katarzyna Kotulska-Jozwiak

The Children's Memorial Health Hospital, Warsaw, Poland

We would like to discuss a case of a girl who has been admitted to our hospital for presurgical evaluation and remains a diagnostic and therapeutic challenge.

She's been suffering from epilepsy since being 18 months – at first presenting with unprovoked, sporadic GTCS. No correlation with fever or infection. Until the age of 10 no AED was introduced and no seizures were reported. Her intellectual development was rated as above-average. After the seizure-free period the seizures recurred, described by the mother as: 1 - difficulties speaking and eyelid fluttering, lasting 20-30 minutes every evening; 2- tremor of the left hand with preserved consciousness, occurring couple of times a week. In the medical files we found description of episodes of strange feelings like elongation of her nose or the right hand. The EEG recordings (interictal) always showed generalized changes, also with a pattern of typical 3Hz discharges. The MR exams at first showed no changes. Metabolic tests were not significant. No genetic testing performed. She has been treated with VPA, LEV, TPM, LAC, LTG, CLB and solumedrol pulses with no significant effect. The last MR exam (2018) suggested pathological focus in the right parahippocampal gyrus. In FDG-PET exam decreased FDG uptake in the medial part of the right

temporal lobe was described.

In our department we performed a 15-hour video-EEG (on VPA+LTG+CLB treatment) with registration of three clinical episodes lasting about 30 minutes each. During those events the girl was responsive, but had difficulties speaking with lower reaction time and slower speed of speech. When in standing position she had tendency to fall down, like having "weak knees". No lateralizing signs could be noticed. At the time of clinical symptoms we registered runs of generalized waves around 14Hz and amplitude 30-80uV with superimposed synchronized sharp waves and sharp-slow wave discharges, evolving into continuous generalized discharges of sharp and slow wave complexes 2-2,5Hz and amplitude up to 320uV. No significant effect after diazepam application.

We introduced MAD with uncompliance. Now the girl is put on ESM. We expect the results of genetic testing (1000 genes panel) in April.

P27

Penelope syndrome: Exploring the Pandora's Box of Genetic Associations

Asuri Prasad, Natalya Karp, Ahmad Alanezi, Craig Campbell, Andrea Andrade

Western University/schulich School Of Medicine & Dentistry, London, Canada

Background: Penelope syndrome is identified by the defining characteristic EEG features of continuous spikes and waves, or status epilepticus, during sleep (SES). SES is associated with acquired epileptic aphasia, cognitive and behavioral disturbance, as well as motor impairment. In addition to organic brain lesions, genetic underpinnings are being identified.

Methods: We present two siblings, their father who were identified with features of epileptic aphasia, language disturbance and focal epilepsy, and a child with chromosomal aberration. In 2 of the 3 children a distinctive pattern consistent with SES was identified during EEG monitoring.

Results: The first patient presented with focal onset seizures at age 3 years accompanied by language and cognitive regression, EEG features consistent with SES. She was treatment resistant with conventional anti-epileptic medications, but responded well to steroids regaining language developmental milestones. Her 5-year-old sister presented with focal onset seizures. Her language

development shows impairments in receptive language functions. A previously unreported potentially pathogenic GRIN2A variant was identified in the 2 siblings and their biological father. The third child initially presented with focal seizures with EEG correlates, developmental impairments in language, cognition and behavior. During follow up, she too exhibited EEG features of SES and treatment resistance. She was identified to have a 16p11.2 microduplication on a chromosomal microarray.

Conclusion. GRIN2A (16p13.2) codes for a subunit of the NMDA receptor, and is known to be associated with variant phenotypes of focal epilepsy and Landau Kleffner syndrome. Several candidate genes in the interval of 16p11.2 gain (SEZ62, DOC2A, and others) expressed in the developing brain may provide insights into a gene dosage effect resulting in SES.

P28

Encephalopathy with Super Refractory Status Epilepticus Related to Chemotherapy in a Young Patient with Osteosarcoma

Maria Grazia Celani¹, Lorenza Di Genova³, Katia Perruccio², Maurizio Caniglia², Susanna Esposito³, Teresa Anna Cantisani¹

¹Neurofisiopatologia, Azienda Ospedaliera di Perugia, Perugia, Italy, ²Oncoematologia Pediatrica, Azienda Ospedaliera di Perugia, Perugia, Italy, ³Clinica Pediatrica, Azienda Ospedaliera Universitaria, Perugia, Italy

Background: Neurotoxic side effects (SEs) of chemotherapy occur frequently. Chemotherapeutic agents may cause both peripheral and central neurotoxicity. Incidence of neurologic syndromes with Methotrexate (MTX) covers a range from 2.3% to 15% and are frequently central. Cisplatin (CDDP) mostly induces peripheral neurological damage, albeit in adults there have been several reports on central neurotoxicity, induced seizures have been estimated at 10% and occur from 6h to 3 months after treatment onset. Only very few cases of severe neurologic central dysfunction following chemotherapy have been reported in children.

Methods: We describe a case of a young patient affected by osteosarcoma treated with chemotherapy and complicated by an acute encephalopathy characterized by super refractory epileptic status and altered mental status with aggressive behaviour and hallucinations.

Results: 13-year-old male with primary high-grade osteosarcoma of tibia received MTX and CDDP containing

polychemotherapy. He developed fever, confusion, psychomotor agitation and non-convulsive epileptic seizures after the first course of drugs administration (MTX 12 g/sm; CDDP 120 mg/sm). Imaging, lumbar puncture and laboratory values were within normal limits, EEG revealed frontal status epilepticus that persisted despite lorazepam IV, phenytoin IV and oral oxcarbazepine administered at increasing dose; only after high dose of continuous IV midazolam there was a good clinical and electrical improvement; SE recurred on weaning of midazolam. At this point, to switch from IV to oral therapy, high oral lorazepam dose every 4 h/day was started. After a week EEGs were without paroxysmal discharges. His mental status improved after risperidone although it is an off label use. After two months, his osteosarcoma was treated with surgical resection. As well as a very good response was achieved (post-chemotherapy necrosis grade: 99%), he received further courses of low-dose cisplatin (80 mg/sm) and methotrexate (8 and 10 g/sm), with no further seizures. He currently is on antiepileptic and anti-psychiatric therapy.

Conclusions: Health providers should be aware of the potential central neurotoxicity associated with chemotherapy in children, after excluding other causes (metastasis, cerebrovascular accident, venous thrombosis, paraneoplastic syndromes, infective complications). Understanding the mechanism and predictors neurotoxicity is important to improve treatment outcomes in paediatric patients.

P29

Prolonged repeated episodes of non convulsive status epilepticus with slight cognitive impairment in a 71 yo man

Valtere Merella, Marta Melis

Neurology Dept Azienda ospedaliera "G. Brotzu", Cagliari, Italia

Background: "Non-convulsive status epilepticus (NCSE) is one of the great diagnostic and therapeutic challenges of modern neurology. Because the clinical features of this disorder may be very discrete and sometimes hard to differentiate from normal behaviour, NCSE is usually overlooked and consequently not treated properly".

Methods and Results : We report the case of a 71 years old health man (only hypertension) that, during last 5 years, presented at least 2-3 episodes/year of slight confusional state. The wife referred that the husband showed events – lasting until 2 days - characterized by mild confusional

state. During these events he had difficulty to: a) find objects of common daily use, b) maintain goals of ordinary decisions and projects and c) assume usual daily therapy. He was admitted in our Neurology Dept. only when, during last episode (Jan. 13, 2019), he presented a tonic-clonic seizure. EEG done when admitted in our dept. showed subcontinuous polyspike and wave bilateral discharges (2-3Hz) interrupted by normal alpha activity; bolus of 1000 mg Levetiracetam i.v. infusion in 5' reduced gradually activity frequency with progressive prolonging of normal pattern intervals (from 2" until 20" and more).

Brain TC, routine haematochemical examination, EKG were normal. No fever or use of psychotropic drugs/substances assumption. Cognitive and brief term memory were normal before and after LEV. Brain MRI will be done next week.

Conclusions: we report the case to reflect about opportunity to recur to aggressive treatment during NCSE and how long extend aed therapy in an apparent non symptomatic. Finally, may we consider our case a recurrent absence status with in consideration of slight compromise of daily performances?

References

- 1) NCSE in adults: H Meierkord, H Holtkamp, Lancet Neurology, apr. 2007
- 2) Recurrent status epilepticus as the primary neurological manifestation of CADASIL: A case report. Epilepsy and Behaviour case report, vol.3, 2015

P30

Correlation between initial clinical and electroencephalographic findings and follow-up of elderly with nonconvulsive status epilepticus

Gloria Maria Tedrus, Mariana Vidal

Pontifícia Universidade Católica De Campinas, Campinas, Brazil

Background: There are controversies concerning ictal EEG patterns and therapy procedures for the treatment of nonconvulsive status epilepticus (NCSE). **Objective:** To correlate clinical and ictal EEG data after administration of benzodiazepine (BZD) and/or antiepileptic drugs (AEDs) in elderly individuals with NCSE diagnosis, in accordance with ILAE, at a significance level of $p < 0.05$.

Procedures: Thirty-six elderly patients (70.8 ± 7.8 years) with clinical manifestation and critical record of NCSE, treated at the PUC Hospital, Campinas, SP, Brazil, were

included in the study.

Results: Eight patients with NCSE with coma and 28 patients with NCSE were not comatose. Change in basal activity occurred in 30 cases, rhythmic delta activity (RDA) occurred in 13 cases and periodic patterns (PD) occurred in 19 cases (lateralized in 18 cases and generalized in 1 case), and electrographic SE was observed in 13 (53.1%) cases. Initial clinical improvement after BZD and/or antiepileptic drug (AEDs) therapy was observed in 20 (52.6%) cases; improvement in EEG background activity occurred in 10 (27.8%) cases and in EEG patterns in 20 (55.6%) cases after 3.9 days. A total of 14 deaths occurred. No significant association was observed between initial clinical improvement and background activity improvement (Fisher's exact test, $p = 0.456$) and EEG patterns (RDA, PD, unequivocally clear focal electrographic SE) ($p = 0.091$), death ($n = 9$ vs $n = 5$, $p = 0.501$) and presence of acute or remote brain injury. The predictive factor for the occurrence of death was the diagnosis of NCSE in comatose patients ($p = 0.016$).

Conclusion: No specific electrographic discharge patterns were observed according to the type of NCSE. No relationship between EEG patterns and initial clinical improvement after BZD/AED therapy was observed in elderly patients with NCSE. Death rate was high and related to NCSE with coma.

Keywords: non-convulsive status epilepticus, EEG, elderly.

P31

Electroencephalographic status epilepticus is common in critically ill children undergoing continuous EEG monitoring

F Fung, M Jacobowitz, L Vala, D Parikh, M Donnelly, M Fitzgerald, S Massey, A Topjian, N Abend

Children's Hospital of Philadelphia and the University of Pennsylvania, Philadelphia, United States

Objectives: Electroencephalographic seizures are common in critically ill children undergoing continuous EEG monitoring. However, few data are available regarding seizure characteristics which would inform management decisions. We aimed to describe electroencephalographic seizure characteristics with management implications.

Methods: We performed a single-center prospective observational study of consecutive critically ill children undergoing continuous EEG monitoring.

Results: This interim analysis included 498 consecutive critically ill children who underwent EEG monitoring from April – November 2017. Subjects were 56% male, the median (IQR) age 5.9 years (1.5, 13.1), and categorical diagnoses included acute structural (40%), acute non-structural (30%), and epilepsy-related (30%). Electrographic seizures occurred in 137 (28%) patients. Seizure duration was less than 1 minute in 69 subjects (51%), 1-5 minutes in 39 subjects (29%), 6-30 minutes in 17 subjects (13%), and >30 minutes in 10 subjects (7%). Electrographic status epilepticus occurred in 29 subjects (21%) and consisted of continuous seizures in 9 subjects (31%) and frequent recurrent seizures in 18 subjects (62%). Seizure onset was focal in 69 subjects (51%), generalized in 63 subjects (46%) and multifocal in 4 subjects (3%). Seizure spread was focal/unilateral in 51 subjects (37%) and bilateral in 85 subjects (62%).

Conclusions: Electroencephalographic status epilepticus is common and has been associated with unfavorable neurodevelopmental outcomes. However, brief seizures (< 1 minute) are also very common. These seizures may not induce secondary brain injury may not provide benefit while exposing patients to unnecessary anti-seizure medication adverse effects. Further studies are warranted to determine the optimal management of seizures of varying durations.

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The EEG diagnosis of NCSE: concordance between Salzburg Criteria and clinical practice

Giada Giovannini¹, Alshimaa Othman², Niccolo' Orlandi^{1,3}, Stefano Meletti^{1,3}

¹Unit of Neurology, OCSAE Hospital, AOU, Modena, Italy, ²Kasr-Alainy School of Medicine, Cairo University, Cairo, Egypt, ³Department of Biomedical, Metabolic and Neural Sciences; Center for Neuroscience and Neurotechnology, University of Modena and Reggio Emilia, Modena, Italy

Background: The diagnosis of Non Convulsive Status Epilepticus (NCSE) in everyday clinical practice can be challenging. To help identify NCSE, Salzburg criteria (SC) have been recently validated. Here we evaluate the concordance in NCSE diagnosis between neurologists not trained in SC use, who take care of the patient in the clinical setting, and an expert panel who retrospectively

evaluated the EEG according to SC.

Methods: All consecutive urgent EEG done from January 1st to March 30th 2018 were considered.

A pool of three epileptologists trained in the use of SC, and not involved in the clinical evaluation of the incident case (and of the corresponding EEG), retrospectively classified the EEG pattern according to SC in three categories: definite NCSE, no NCSE, possible NCSE. Finally, we defined the degree of concordance between the diagnosis made by the neurologist who took care of the patient and the classification made by the expert.

Results: Among the 574 consecutive EEG done in emergency conditions in the examined period, 187 (33%) have been made to rule out a NCSE (105 male; median age of 73 yrs) and were evaluated by 15 physicians. The neurologist made a diagnosis of NCSE in 19 (10%) out of 187 cases. The expert panel classified 9 EEG (5%) as "definite NCSE", 96 (51%) as "no NCSE" and 82 (44%) as "possible NCSE". Among the 82 cases defined as "Possible NCSE" by the expert, 10 (12%) were diagnosed as NCSE, while 72 (88%) were considered without status. Concordance was 100% evaluating the "no NCSE" and the "definite NCSE" categories.

Conclusions: our data show that there is a considerable discrepancy between diagnosis made by neurologists not trained in the use of SC and the expert panel. The "Possible NCSE" category is a grey zone and further studies are needed.

P34

Retrospective study of three NORSE cases: EEG features and treatment

Debora Andrade, Fabio Abreu, Zaloa Agirre-Arrizubieta

King's College Hospital NHS Foundation Trust, London, United Kingdom

Background: New-onset refractory status epilepticus (NORSE) is a clinical presentation in which patients without a history of Epilepsy suddenly develop prolonged seizures that do not respond to at least two standard anti-epileptics (AEDs) and for which the cause for the seizures remains unidentifiable beyond 72 hours. Clinicians' aim is to treat the possible cause, suppress the seizures and aim for suppression burst (SB) in EEG which has been found to be associated with less breakthrough seizures and with no increased rate of intra-hospital complications. Multi-disciplinary ward rounds are essential to avoid increasing morbidity.

We analyse the clinical care and outcome of the patients that presented with NORSE at King's College Hospital, London, UK.

Methods: This is a retrospective study of three patients who presented with NORSE during the last four consecutive years at King's College Hospital. Review of clinical notes and multi-disciplinary ward rounds are performed.

Results: The three patients were under 35. Mean length of admission in ICU was 11 days. Extensive diagnostic check list was performed. Suppression burst was achieved promptly, 0-3 days, administering 5 anaesthetics drugs and 4 AEDs. Immuno-modulation therapies were also provided. Breakthrough seizures, clinical and electrographic, reappeared within a mean of 9 days (0-22). The three patients died. The post-mortem reports could not identify the primary cause for NORSE in two patients and identified resolving encephalitis with ischaemic changes in one patient.

Conclusions: Despite achieving SB promptly, breakthrough seizures reappeared and despite multi-disciplinary ward rounds and different approaches of treatment, the three patients died. The early identification and treatment of seizures did not seem to be associated with a good outcome. Hence, the best management and treatment of NORSE remains difficult to determine. Are seizures an epiphenomenon of a more diffuse clinical entity? Should we be focusing and treating every detected seizure? Further studies with larger sample of patients' data would be helpful to agree a diagnostic and treatment pathway, and to analyse possible aetiologies that might benefit from aggressive treatment compared to others.

P35

The Spectrum of Electrographic Seizure Patterns in the Critically Ill

Deepa Panjeti-Moore¹, Nabil T Makhoulouf¹, Assad Amin², Shanaz Merchant¹, Monica B Dhakar¹, Andres A Rodriguez Ruiz¹, Ioannis Karakis¹, Hiba A Haider¹

¹Emory University Hospital, Atlanta, United States, ²Ohio State University Medical Center, Columbus, United States

Background: Electrographic seizures are common in critically ill comatose or encephalopathic patients. To date, there is little data regarding seizure onset patterns (SOP), seizure onset frequencies (SOF) and other electrographic features of seizures, and whether or not meaningful associations with clinical characteristics exist in this population.

Methods: 44 subjects from 2013 to 2017 were identified from a clinical database of hospitalized patients undergoing continuous video EEG monitoring. All had documented electrographic seizures, and were altered or critically ill. Patients with focal motor seizures with intact awareness were excluded. The definitions for various ictal and periodic/rhythmic patterns were based on published criteria. Board-certified or board-eligible electroencephalographers each reviewed two seizures per patient.

Results: In this cohort of 44 subjects, the mean age was 55.5 years; 40.7% were women. 91 seizures were analyzed. Status epilepticus was present in 55.1% of patients. SOP's were most commonly rhythmic sharp waves or spike-wave complexes, followed by rhythmic evolving activity (35.9%), fast activity (>13 Hz) (12.1%), and attenuation (1.1%).

SOF was delta in 50.5%, theta in 36.3%, alpha in 12.1% and beta in 1.1%. Maximal spatial extent remained localized/focal in 47.3%, hemispheric spread in 36.3%, and generalized in 16.5% of seizures studied.

There was a significant association of SOP with the presence of acute brain injury (Pearson chi square of 9.086, $p < 0.05$) and poor outcome (trend toward significance $p = 0.074$). Higher SOF (alpha or beta) were associated with better outcome (chi 8.208, $p < 0.05$).

There was no significant association of SOP with the presence/absence of status epilepticus, or the use of therapeutic coma.

Conclusions: The most common SOP in our cohort of critically ill altered patients appears to be rhythmic discharges. Majority of seizures were delta frequency at onset and associated with a dichotomous outcome, while higher onset frequencies (alpha or beta) portended a better outcome. Larger prospective studies are further needed to explore electrographic characteristics that may predict a response to treatment or outcome.

P36

Improved outcome on early immunotherapy in new onset refractory status epilepticus (NORSE). Experience in Qatar

Gayane Melikyan^{1,2}, Soha Malki¹, Musab Ali¹, Bolenour Mesraoua^{1,2}, Hassan Al Hail¹, Dirk Deleu^{1,2}, Basim Uthman^{2,1}, Naim Haddad^{2,1}

¹Hamad Medical Corporation, Doha, Qatar, ²WCMC-Q, Doha, Qatar

Introduction: New-onset refractory status epilepticus (NORSE) is defined as refractory status epilepticus without

an obvious cause after initial investigations.. Refractory status epilepticus (SE) is a condition in which patients suddenly experience continuous seizures or a flurry of very frequent seizures that do not respond to standard anticonvulsant medications . Seizures are thought to be due to an excess of pro-inflammatory molecules in the brain, perhaps triggered by a simple viral infection, although no clear cause has ever been demonstrated.

Materials and Methods: This is a descriptive, retrospective review of 10 previously normal adult patients (age between 28 and 56 years) with NORSE admitted to Hamad Medical Corporation MICU in Qatar from 2012 to 2018.

Results: Ten patients with NORSE syndrome were identified, where a cause was not established despite an exhaustive search with an average duration of 27 days (range 14-32). Characterizing features were male gender, young age, previous good health, cerebrospinal fluid pleocytosis (in 7), antecedent febrile illness (in 7), extraordinarily prolonged status epilepticus, failure of extensive investigations to reveal an underlying cause, catastrophic outcome as well as T2 hyperintense signal in temporal lobes (in 5), BL symmetrical putaminal T2/flair high signals (in 1) and leptomeningeal enhancement (in 1) on brain magnetic resonance imaging. Treatment modalities included at least 3 antiepileptic drugs (in all patients), anesthetics (in all patients), intravenous immunoglobulin (IVIG, 8 patients), steroids (4 patients), plasmapheresis (1 patient). Five patients improved completely without neurological deficit and three of them survived with moderate to severe disability. Two patients who were not given early immunotherapy, died from complications associated with prolonged ICU stay. One of the survivors received long term immunotherapy.

Conclusions: The cause of NORSE syndrome may often be difficult to find. NORSE carries a poor prognosis and early recognition and treatment may improve outcomes. Epilepsy and cognitive issues are common among survivors although a small minority of them eventually return to a normal lifestyle. Affected individuals are most often treated for weeks in an intensive care unit because they require prolonged anesthesia to control their seizures. In this case series, we have shown that immunotherapy seems to be a helpful treatment option when conventional therapy fails.

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Association between initial therapy of refractory generalized convulsive status epilepticus in adults and its outcome.

Pavel Vlasov, Boris Gladov, Tatiana Pushkar

Moscow State University Of Medicine And Dentistry Named After A.I. Evdokimov, Moscow, Russian Federation

Objective: to analyze outcomes of refractory (R) generalized convulsive status epilepticus (GCSE) in adults.

Materials and Methods: The study included 23 women with RGCSE, aged from 19 to 76 years. Patients presented with RGCSE in acute symptomatic form (n = 5) and as a complication of epilepsy (n=18), of them 14 with structural focal epilepsy, 3 with focal epilepsy of unknown etiology, 1 with combined idiopathic generalized and structural focal epilepsy. Intravenous (iv) ivLorazepam, ivPhenytoin, ivPhenobarbital are unavailable in Russia, however iv Diazepam (ivDZP), Valproic Acid (ivVPA), Levetiracetam (ivLEV), Lacosamid (ivLCM) and iv anesthetics are available. Initial GCSE treatment for patients at home and in an ambulance was started with ivBZD, with ivVPA, or with combination of ivBZD+ivVPA within 35 min to 150 min after the GCSE onset. The maximum dose (mg/kg) of all types of ivAEDs and iv anesthetics was used.

Results: 3 patients (13%) with acute symptomatic GCSE died due to multiple organ failure not related to GCSE. In the remaining 18 cases, RGCSE was relieved. Non-acute symptomatic RGCSE lasting for 3 to 132 hours was observed mainly in structural focal (frontal, fronto-temporal) epilepsy (60.9%). The main reason for the development of GCSE in adults (43.5%) was an AED withdrawal. In these cases, the basic oral AEDs were continuously administered through a naso-gastric tube. Super-refractory GCSE was confirmed in 11 cases (47.8%). In the prehospital phase of GCSE treatment, ivDZP was used in 6 patients, 5 of them developed super-refractory GCSE; ivVA was used in 8 patients, 2 of them developed super-refractory GCSE; initial therapy with ivDZP+ivVA was used in 7 patients, 3 of them developed super-refractory GCSE. During treatment with iv anesthetics, respiratory depression developed with subsequent invasive ventilation and longer recovery. In one case of RGCSE recurrence, perampanel was successfully administered through a naso-gastral tube at 12 mg/day.

Conclusions: deaths occurred only in cases of acute symptomatic RGCSE. The vast majority of refractory RGCSE in adults (43.5%) was provoked by withdrawal of AEDs. Preliminary results indicate that prehospital (initial) use of ivVPA or a combination of ivDZP+ivVA significantly increase the efficacy of RGCSE therapy.

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Prognosis in patients with brain tumor-associated status epilepticus

Laura Abraira Del Fresno¹, Manuel Toledo¹, Maria Sueiras², Lorena Guzman², Manuel Quintana¹, Fran Martínez-Ricarte³, Esteban Cordero³, Elena Martínez-Saez⁴, Jessica Camacho⁴, Javier Salas-Puig¹, Estevo Santamarina¹

¹Epilepsy Unit, Neurology Department, Vall D'hebron University Hospital, Barcelona, Spain, ²Neurophysiology Department, Vall d'Hebron University Hospital, Barcelona, Spain, ³Neurosurgery Department, Vall d'Hebron University Hospital, Barcelona, Spain, ⁴Anatomical Pathology Department, Vall d'Hebron University Hospital, Barcelona, Spain

Background: Tumor related epilepsy is common in patients with brain tumors and it usually starts at the onset of the disease. By contrast, status epilepticus is less frequent, occurs at later stages and it is often related with tumor progression. We aimed to investigate prognosis and associated factors in these patients.

Methods: We consecutively included 61 patients that were admitted at our hospital due to brain tumor-associated status epilepticus between 2011-February and 2018-April. Demographic and clinical characteristics (type of tumor, duration and treatment of the status epilepticus) were recorded. We analyzed status epilepticus prognosis at long-term (GOSE – Glasgow Outcome Scale) and related factors.

Results: Mean age was 62.64 years-old (± 14.9) and 59% were men. The 34.4% (n=21) were metastasis, followed by meningiomas (24.6%, n=15), glioblastoma multiforme (24.6%, n=15), low grade glioma (4.9%, n=3) and other (11.7%, n=7). Mean follow up was 12.6 months and mean survival time 19.6 months (IC 11.4-27.4). On the multivariate analysis the presence of glioblastoma multiforme or metastasis (OR 19 (2.23 – 161.58), p=0.007) and the status epilepticus duration >18 hours (1.28 – 42), p=0.025) independently predict worse prognosis at one year follow-up. Mortality at follow up was only associated with the type of tumor (HR 7.26 (2.59-20.37), p<0.001)

Conclusions: Longer duration of status epilepticus and the presence of glioblastoma multiforme or metastasis predict poor prognosis at long-term.

P39

Impact of epileptic seizures in the neurological intensive care unit (NICU) on Glasgow Coma Scale (GCS)

Gursimran Singh, Birinder Paul, Ashwani Chaudhary, Gagandeep Singh

Dayanand Medical College and Hospital, Ludhiana, India

Background: Neurological patients frequently require glasgow coma scale monitoring at regular intervals. In intensive care units there are many patients admitted for monitoring of their consciousness. Seizures are associated with loss of consciousness if they are generalized. Quite often patients in the neurological intensive care units are monitored due to the underlying neurological disorder. The Glasgow coma scale is an extremely useful method of monitoring and prognosticating patients in the neurological ICU. Hence the occurrence of seizure with loss of consciousness might confound the assessment of Glasgow coma scale

Materials and methods: It is a prospective observational study with a control arm. Subjects were enrolled if they had a seizure during admission to Intensive care unit (neurology and neurosurgery). Baseline GCS of all patients (n=50) who develop/manifest a clinical seizure was monitored for 48 hours. Controls (n=50) were matched with the baseline GCS of cases. The difference in GCS of both the patients at the specified interval was noted. Cases and controls are then compared on basis of their clinical profile and the assessment of GCS readings.

Results: Mean of the baseline GCS of cases was 10.44 (SD 3.79) and just after seizure was 5.82 (SD 2.96) at 2 hours was 7.8 (SD 3.87), at 4 hours was 8.48 (SD 4.21), 8 hours was 8.74 (SD 4.44), 12 hours was 8.9 (SD 4.59), 24 hours was 8.86 (SD 4.62) and at 48 hours was 9.06 (SD). In controls mean of the baseline GCS is 10.5 and it remained 10.5. The most common time interval when the patient did return to the baseline Glasgow coma scale rating was 2 hours.

Conclusion: Seizure will confound the GCS of a patient but maximum will return to baseline consciousness level. Some patients did not return to baseline GCS and presence of status epilepticus in infectious or inflammatory encephalitis was important treatable cause.

P40

EEG Features for Outcome Prediction After Cardiac Arrest in Children

France Fung, Alexis Topjian, Rui Xiao, Nicholas Abend

Children's Hospital of Philadelphia and University of Pennsylvania, Philadelphia, United States

Background: In-hospital cardiac arrest occurs in over 10,000 children per year in the United States, with high neurobehavioral morbidity amongst survivors. Early assessment of brain injury severity is important for neuroprognostication. However, clinical and resuscitation variables do not directly assess brain function and therefore may not optimally predict neurobehavioral outcomes. We aimed to determine which EEG features and feature combinations most accurately predicted short-term neurologic outcomes and survival in children resuscitated after cardiac arrest.

Methods: Prospective single-center observational study of children resuscitated from cardiac arrest who underwent conventional EEG monitoring with standardized EEG scoring. Logistic regression evaluated the marginal effect of each EEG variable or EEG variable combinations on the outcome. We identified the models with the highest areas under the receiver operating characteristic (AUROC), evaluated the optimal models using a 5-fold cross-validation approach, and calculated test characteristics.

Results: 89 children were evaluated. Unfavorable neurologic outcome (Pediatric Cerebral Performance Category score 4-6) occurred in 44 subjects (49%) including mortality in 30 subjects (34%). A model incorporating a four-level EEG Background Category (normal, slow-disorganized, discontinuous or burst-suppression, or attenuated-flat), Stage 2 Sleep Transients (present or absent), and Reactivity-Variability (present or absent) had the highest AUROC. Five-fold cross-validation for the optimal model predicting neurologic outcome indicated a mean AUROC of 0.75 (range 0.70-0.81) and predicting mortality indicated a mean AUROC of 0.84 (range 0.76-0.97). The specificity for unfavorable neurologic outcome and mortality were 95% and 97%, respectively. The positive predictive value for unfavorable neurologic outcome and mortality were both 86%.

Conclusions: The specificity of the optimal model using a combination of EEG features was high for unfavorable neurologic outcome and death. However, the positive predictive value was only 86% for both outcomes. Therefore, EEG data must be considered together with the overall clinical context.

P41

Factors predicting cessation of status epilepticus in clinical practice – data from a prospective observational registry (SENSE)

Christoph Kellinghaus^{1,2}, Andrea O. Rossetti³, Eugen Trinka^{4,5}, Nicolas Lang⁶, Theodor W. May⁷, Iris Unterberger⁸, Stephan Rüegg⁹, Raoul Sutter^{9,10}, Adam Strzelczyk^{11,12}, Christian Tilz¹³, Zeljko Uzelac¹⁴, Felix Rosenow^{11,12}

¹Klinikum Osnabrück, Osnabrück, Germany, ²Epilepsy Center Münster-Osnabrück, Osnabrück, Germany, ³Department of Clinical Neurosciences, CHUV and University of Lausanne, Lausanne, Switzerland, ⁴Department of Neurology, Christian Doppler Klinik, Paracelsus Medical University, Salzburg, Austria, ⁵Centre for Cognitive Neuroscience, Salzburg, Austria, ⁶Department of Neurology, University Hospital Schleswig-Holstein, Campus Kiel, Kiel, Germany, ⁷Society for Epilepsy Research, Bielefeld, Germany, ⁸Department of Neurology, Innsbruck Medical University, Innsbruck, Austria, ⁹Department of Neurology, University Hospital Basel, Basel, Switzerland, ¹⁰Medical Intensive Care Units, University Hospital Basel, Basel, Switzerland, ¹¹Epilepsy Center Hessen - Marburg, Department of Neurology, University Hospitals and Philipps-University Marburg, Marburg, Germany, ¹²Epilepsy Center Frankfurt Rhein-Main, Department of Neurology, University Hospital Frankfurt and Goethe University, Frankfurt/M, Germany, ¹³Department of Neurology, Krankenhaus Barmherzige Brüder, Regensburg, Germany, ¹⁴Department of Neurology, University Hospital Ulm, Ulm, Germany

Background: Several randomized controlled trials of the efficacy of initial status epilepticus (SE) treatment have estimated success rates of 40–80%. However, observational studies suggest lower proportions. We investigated the initial SE termination rate in a large multinational observational study, and explored variables associated with it.

Methods: Data of adults treated for SE were collected prospectively in centers in Germany, Austria, and Switzerland, during 4.5 years. Incident episodes of 1,049 patients were analyzed using uni- and multivariate statistics to determine factors predicting cessation of SE within 1 hour (for generalized convulsive SE, GCSE) and 12 hours (for non-GCSE) of initiating treatment.

Results: The median age at SE onset was 70 years; the most frequent etiology was remote (32%), followed by acute (31%), or a combination of acute and remote factors (10%). Semiology was generalized convulsive in 43%, focal motor in 28%, and non-convulsive in 29%. Median latency between SE onset and first treatment

was 30 minutes in GCSE and 150 minutes in non-GCSE. The first intravenous compound was a benzodiazepine in 86% in GCSE, and 73% in non-GCSE. Bolus doses of the first treatment step were lower than recommended by current guidelines in 76% of the GCSE patients and 78% of the non-GCSE patients. In 319 GCSE patients (70%), SE was ongoing 1 hour after initiating treatment, and in 342 non-GCSE patients (58%) 12 hours after initiating treatment. Multivariate Cox regression demonstrated that the use of benzodiazepines as first treatment step, and a higher cumulative dose of anticonvulsants within the first period of treatment were associated with shorter time to cessation of SE for both groups.

Conclusions: In clinical practice, treatment guidelines were not followed in a substantial proportion of patients. Our data suggest that benzodiazepines should be used as first treatment step and with a sufficient cumulative dose.

P42

Long term cognitive outcome in adult and adolescent FIRES and NORSE patients

Robert Daniel Nass, Julia Taube, Christian E. Elger, Rainer Surges, Christoph Helmstaedter

Bonn University Hospital, Bonn, Germany

Background: Febrile illness related epilepsy syndrome (FIRES) is a rare and devastating subtype of new onset refractory status epilepticus (NORSE). Little is known about the long term outcome in adolescent and adult survivors. The aim of this pilot study was to identify factors associated with the long-term outcome in important aspects of daily life and cognition.

Methods: Retrospective chart review 2005-2019, clinical interview during routine visits and follow-up between 3 to 5 years after onset. Assessment of various clinical and outcome parameters: global assessment of severity of epilepsy (GASE), modified Rankin scale (MRS) and scores of independence for neurologic and geriatric rehabilitation (SINGER). Results are reported as means (with lower - upper 95% confidence intervals) or frequencies.

Results: We identified 9 patients who fulfilled the criteria of FIRES syndrome survivors. Only two were diagnosed with FIRES at the time, the others as autoimmune encephalitis. Mean age at onset was 27 years (range, 17-37). One patient developed non convulsive, prolonged refractory SE (PRSE), two persistent refractory SE (PRSE) and six persistent, super refractory SE (PSRSE). CSF pleocytosis was reported in 8/9 cases with 63 (4-123) leukocytes/ μ l.

All patients received benzodiazepines and intravenous anticonvulsants prior to anesthetics and intubation. They spent 53 days (27-79) in intensive care. They were seen by us 21 (2-40) months after discharge from the ICU. Outcomes varied with a favorable outcome (MRS=1) in one case, moderate outcomes in seven cases (MRS=2-3) and unfavorable outcome (MRS=4) in one case. One patient had a mild epilepsy (GASE=3), three had moderate epilepsy (GASE=4) and two more severe outcomes (GASE=5-6). Long term SINGER assessment included 7/9 patients. Two patients reported mild, three moderate and three only mild cognitive impairment. Problems with interpersonal communication were reported in two cases.

Conclusions: Long term evaluation of cognitive outcome in patients with FIRES showed that the majority of patients lost independence in daily functioning due to persisting seizures and cognitive. As the condition is very rare, we propose collaborative projects, to investigate factors for a favorable / unfavorable long-term outcome in NORSE/ FIRES survivors.

P43

Terminating pattern of ictal high-frequency oscillations is associated with short-term recurrence of seizures

Yingchi Fan¹, Cheng-Siu Chan², Syu-Jyun Peng², Yue-Loong Hsin¹

¹Department of Neurology, Chung Shan Medical University and Chung Shan Medical University Hospital, Taichung City, Taiwan, ²Biomedical Electronics Translational Research Center, National Chiao Tung University, Hsinchu, Taiwan

Background: It is not uncommon to meet a patient who experiences short-term seizure recurrence after long-term seizure freedom. In case of seizures recurring within a short interval as status epilepticus that will be life-threatening. Pathologic high-frequency oscillations (HFOs) have been linked to ictogenesis. The HFOs encompassing ripples (80–200 Hz) and fast ripples (250–500 Hz) are now known to represent neurophysiologic activities of GABAergic interneurons and glutamatergic principal neurons respectively. In this study, our objective is to address the mutual interaction of ripple and fast ripple in the seizure offset.

Methods: The brain signals derived from patients with drug-resistant epilepsy underwent chronic intracranial recording for epilepsy surgery were analyzed. We categorized high frequency of seizure occurrence (inter-seizure interval less than 4 hours) as clustered seizure

group and lower reoccurrence (seizures separated by over 4 hours and the terminal seizure in a cluster) as isolated seizure group. The intracranial signals were filtered (80-200 Hz and 250-500 Hz) and calculated the rates of HFO. One oscillatory event in each frequency band needed at least four consecutive cycles having an amplitude of 3 standard deviations above the mean of the reference period (a 60-second section 2 minutes before a seizure). The time lag between two consecutive cycles ranges from 5 to 12.5 ms for ripples and from 2 to 4 ms for fast ripples. The HFO distribution during the ictal and postictal (60 seconds) periods was normalized into 100 bins. We then compared the rate of occurrence of ripples and fast ripples using Wilcoxon signed-rank tests followed by Bonferroni-Holm corrections to correct for multiple comparisons.

Results: Forty seizures (24 in isolated group, 16 in clustered group) from 8 patients were analyzed. All seizures were manifested with low-voltage fast at onset, irregular spiking and polyspikes bursting. The mean duration of clustered seizures was shorter. Before seizure offset, the fast ripple activity kept highly and ceased abruptly in the isolated group. But in the postictal period, fast ripple didn't remain silence in the clustered group ($p < 0.01$).

Conclusion: Different patterns of HFO occurrence associate with the mechanisms of seizure termination and clustering.

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withdrawn

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Severity of SE and number of complications in treatment predict mortality at 1 year after SE

Kati Tuppurainen¹, Jaakko Ritvanen¹, Harri Mustonen², Leena Kämppi¹

¹Clinical Neurosciences, Neurology, Department of Neurology, University of Helsinki and Helsinki University Central Hospital, Helsinki, Finland, ²Department of Surgery, University of Helsinki and Helsinki University Central Hospital, Helsinki, Finland

Background: Status epilepticus (SE) is a life-threatening neurologic emergency which requires prompt medical treatment. Little is known of the long-term survival of SE. The aim of this study was to investigate which factors influence the 90 day and 1-year mortality after SE.

Methods: This retrospective study includes all consecutive adult (>16 years) patients (N = 70) diagnosed with GCSE in Helsinki University Central Hospital emergency department over 2 years. We defined specific factors including patient demographics, SE characteristics, treatment, complications and delays in treatment and determined their relation to 90 days and 1-year mortality after SE by using univariate and multivariate regression models.

Results: In-hospital mortality was 7.1%. Mortality rate increased to 14% in 90 days and to 24% in 1 year after SE. In the univariate analysis no previous history of epilepsy ($p=0.014$), STESS >4 ($p=0.012$), long delays in seizure freedom ($p=0.041$) and long delays in gaining consciousness ($p=0.014$) were factors associated with mortality at 90 days. STESS >4 ($p=0.028$) and use of vasopressors ($p=0.049$) were associated with mortality at 1 year.

Trend-like association with 90 days mortality was found in long onset-to-diagnosis ($p=0.054$), onset-to-tertiary-hospital ($p=0.057$), onset-to-burst-suppression ($p=0.085$) times, in long ICU treatment ($p=0.063$), with increasing score in CBI (Complication Burden Index) ($p=0.093$) and achievement of Burst-suppression ($p=0.074$). No previous history of epilepsy ($p=0.053$), increasing score in CBI and long ICU treatment ($p=0.057$) had trend-like association with mortality at 1 year. Multivariate analysis revealed STESS >4 (ODDS 16.68, $p=0.002$) to be associated with mortality at 90 days. STESS > 4 (ODDS 11.39, $p=0.001$) and increasing score in CBI (ODDS 1.5, $p=0.05$) were associated with mortality at 1 year.

Conclusions: While delays in treatment have been associated with worse prognosis at hospital discharge in previous studies, other factors seem to influence long-term prognosis of SE. Severe form of SE, etiology other than epilepsy, long ICU treatment and high number of complications predict long term mortality, especially at 1 year after SE. Same factors are associated with mortality at 90 days, though at this point delays in treatment still seem to have an effect.

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Prospective evaluation of ADAN Scale: a tool to a prompt identification of Status Epilepticus (SE)

Estevo Santamarina, Manuel Requena, Elena Fonseca, Laura Abraira, Manuel Quintana, Xavier Salas-Puig, Marta Olive¹, Manuel Toledo¹

Hospital Vall Hebron, Barcelona, Spain

Background: The ADAN scale was designed to select those patients with risk to develop status epilepticus (SE) after experiencing an epileptic seizure. This scale was defined after a retrospective study and it is based on 4 clinical items: Abnormal speech, ocular Deviation, Automatism and Number of motor seizures. However, this scale needs a prospective evaluation and this is the purpose of our study.

Methods: This is a prospective evaluation of all patients arriving at our emergency department with a suspicion of seizure or other neurological symptoms. All these patients were scored using the ADAN scale upon arrival. Afterwards, all patients were evaluated by a neurologist and were performed all necessary ancillary tests; if all the symptoms were not clearly explained by a stroke, they performed an emergent EEG to rule out SE. We ruled out stroke patients for this study.

Results: A total of 128 no-stroke patients were evaluated using ADAN scale upon arrival during 6 months (June - December 2018). Median age was 58.5; 79 (61.7%) were male. 58 (45.3%) had a previous history of epilepsy. Regarding ADAN score: 65 (51,6%) had a low risk for SE (ADAN=0-1) it was 0; 28 (21,9%) had a moderate risk (ADAN=2) ADAN and 34 (26,6%) had a high risk (ADAN>2). After a thorough clinical evaluation and a EEG, 45 (35.2 %) fulfilled criteria for SE. When analyzing the ADAN score and the finding of SE, a score >1 was significantly associated with a diagnosis of SE (69% in ADAN>1 group vs. 3% in ADAN=0-1; p=0.0001). The predictive capacity of the scale for identifying SE in the validation dataset was 95.6%. Taking into account, the different groups according to risk, 85.3 % of high-risk group showed SE, 50 % of moderate-risk group and 3% of low-risk group.

Conclusion: ADAN scale is a strong predictor of the diagnosis of SE in patients who experience an epileptic seizure. This scale may be a useful tool for clinical use in order to help to select patients in high risk of SE, and allow a faster diagnosis and an early treatment.

P47

The outcome of non-convulsive status epilepticus

TD Gosavi^{1,2}, SJ See^{1,2}, Ms Zhi Xuan Ng³, SH Lim^{1,2}

¹National Neuroscience Institute, , Singapore, ²Singapore General Hospital, Singapore, Singapore, ³Yong Loo Lin School of Medicine, , Singapore

Background: It is not entirely clear, to what extent, non-convulsive status epilepticus (NCSE) contributes to clinical impairment and neurological injury. To assess the clinical impact of NCSE, we retrospectively analysed the cases of NCSE in our cohort.

Methods: NCSE episodes diagnosed during electroencephalographic evaluation over a period of three years from January 2012 to December 2014 were identified, and the clinical data of patients was analysed for the admission during which NCSE occurred. Outcomes at discharge were defined as good if the patient was back to baseline functional status or had mild functional decline requiring some rehabilitation; and poor if death occurred or if the patient had significant functional decline.

Results: From 2663 inpatient EEGs done over three years, 81 episodes of NCSE were identified (3.04%). The average age of patients with NCSE was 65 years. 42 were females and 39 males. The mean duration of NCSE was 3.36 days. The average length of inpatient stay during the admission under consideration was 30.66 days. 29(25.8) had a primary neurological cause for NCSE, 15(18.5%) had a systemic (metabolic/septic/toxic) cause, and 36(44.4%) had both. 23(28.4%) were known to have epilepsy prior to the NCSE episode.

35(43.2%) had a good outcome at discharge, whereas 46(56.8%) had a poor outcome. It was apparent that the poor outcome was unrelated to the NCSE itself, from the wide difference in the averages of length of hospital stay and length of NCSE itself, and there being no relation between the number of antiepileptic drugs used or anaesthetic agent usage (midazolam in most cases) with the outcome.

Factors associated with poor outcome were no prior epilepsy (OR 3.85; 95% CI 1.26 to 1.78; p=0.01); no episode of clinical seizure associated with NCSE (OR 4.06; 95% CI 1.41 to 11.6; p=0.009) and NCSE due entirely to systemic causes (OR 3.2; 95% CI 0.97 to 10.45; p= 0.05).

Conclusion: In our cohort, outcome of NCSE is poor and is likely to be influenced by the nature of underlying illness rather than NCSE itself. NCSE in patients with epilepsy and NCSE associated with an episode of clinical seizure have a better outcomes.

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Therapy of non-convulsive status epilepticus in severe brain injury

Ekaterina Povaliukhina¹, MD Michail Aleksandrov¹, PhD Tatyana Aleksandrova², MD Aleksey Ulitin¹

¹Almazov National Medical Research Center, Polenov Neurosurgical Research Institute (branch, Clinic) , Saint-Petersburg , Russian Federation, ²St. Petersburg Research Institute of Emergency Care named after I.I. Dzhanelidze, Saint-Petersburg , Russian Federation

Background: The study is intended to analyze the effectiveness of levetiracetam, valproic acid and carbamazepine in the treatment of non-convulsive status epilepticus in patients with severe brain injury.

Methods. The results of 30 patients' treatment (26 men, 4 women) aged from 20 to 65 years with severe traumatic brain injury who were examined and treated at the St. Petersburg Research Institute of Emergency Care named after I.I. Dzhanelidze are considered. The level of patients' consciousness was assessed on a Glasgow Come Scale. EEG registration was performed on the "Mitsar-EEG-202" complex in the standard derivations of "10-20%" system. Bandwidth: 1.6 - 35 Hz. EEG monitoring was performed in order to diagnose non-convulsive status epilepticus, in the dynamics with administration of anticonvulsant therapy and clear consciousness. The first group included 12 patients who received carbamazepine at a daily dose of 1200 mg. In the second group of 7 patients, carbamazepine was replaced by levetiracetam with an initial dosage of 2500 mg per day. 11 patients from the third group received valproic acid at a dosage of 1500 mg per day. The significance of differences was assessed using Fisher's exact test.

Results: The level of consciousness of all patients was from coma 1 to coma 2 (from 5 to 8 points GCS, respectively). Among the patients of the first group, carbamazepine was administered immediately after the clinical and electrophysiological verification of the non-convulsive status epilepticus in the initial dosage of 800 mg per day with a gradual increase in the daily dose to 1200 mg. The level of consciousness was restored to clear in 2 of 12 patients (16.7%) for 12-16 days. The apallic syndrome in the outcome was observed in 4 patients. Fatalities occurred in 6 of 12 cases.

In the second group, where carbamazepine therapy was replaced with levetiracetam at a dose of 2500 mg per day, consciousness was restored to a clear in 6 of 7 patients (85.7%) for 6-10 days. One observation was fatal.

In the third group, when confirming the diagnosis of non-convulsive status epilepticus, patients were prescribed

valproic acid at a dosage of 1000-1500 mg per day. Of the 11 patients in this group, in 5 (45.5%), the level of consciousness recovered to a clear in 10-14 days. In three patients, an apallic syndrome was observed in the outcome. Death occurred in three cases.

Thus, the probability of a favorable outcome, consisting in recovery of clear consciousness, was significantly higher (85.7% versus 16.7% and 85.7% versus 45.5%, $p < 0.05$) when levetiracetam was used as anticonvulsant therapy. The duration of unconscious state in patients during the use of this drug was significantly reduced.

Conclusions: Registration of the continued epileptiform activity of a high index on EEG with severe brain injury necessitates the appointment of adequate anticonvulsant therapy in time.

The use of levetiracetam is more effective than the prescription of carbamazepine and valproic acid preparations.

P49

Dosing of anti-epileptic therapy in refractory status epilepticus

Dr. Angela Parsons, Dr. Akta Patel, Dr. Amy Crepeau

Mayo Clinic, Phoenix, United States

Background: Status epilepticus (SE) is a life-threatening condition that if untreated, can lead to significant morbidity and mortality. Goals of SE care begin with patient stabilization followed by first line benzodiazepines. Intravenous anti-epileptic agents can subsequently be used for treatment and in refractory situations, anesthetic agents are necessary. Evidence based guidelines detail appropriate dosing for anti-epileptic treatments in SE. Our aim is to determine whether dosing guidelines are followed in regards to initial anti-epileptic therapy in refractory SE.

Methods: A retrospective chart review was conducted searching for patients aged 18-99 years admitted to Mayo Clinic Arizona over the last 10 years (2008-2018). Refractory SE patients on anesthetic agents during their admission were included in this study. Records were reviewed for initial benzodiazepine and loading doses of anti-epileptic medications at the time of SE identification. Medications reviewed included lorazepam, midazolam, fosphenytoin, levetiracetam, and valproate sodium.

Results: Seventy-six patients were identified with a mean age of 63.1 (27-89). The majority, 50% (38/76), presented in non-convulsive status epilepticus (NCSE). The remaining seizure types included: convulsive SE 25% (19/76),

generalized tonic-clonic seizure followed by NCSE 21% (16/76), and myoclonic seizures 3.9% (3/76). Twenty-five patients had a history of seizure. Forty-seven patients had documented dosing of lorazepam as first therapy with an average dose of 0.05 mg/kg. Average dosing for remaining anti-epileptics included: .09 mg/kg midazolam, 17.8 PE/kg fosphenytoin, 22.5 mg/kg levetiracetam, and 17.5 mg/kg valproate sodium.

Conclusions: SE is life-threatening and requires appropriate dosing of anti-epileptic agents to ensure seizure cessation. Overall, our findings suggest that in general, anti-epileptic agents are underdosed in refractory status epilepticus. Guidelines suggest the following dosing regimens: 0.1 mg/kg lorazepam, 0.2 mg/kg midazolam, 20mg PE/kg fosphenytoin, 60mg/kg levetiracetam, and 40mg/kg valproate sodium. This study provides room for quality improvement in treating patients with SE. Future studies can be done to assess clinical outcomes from better dosing of anti-epileptic therapies.

P50

High-Dose Diazepam Controls Dyskinesia in Anti-NMDA receptor Encephalitis

Hye-Rim Shin, Soon-Tae Lee, Yoonhyuk Jang, Yong-Won Shin, Kon Chu, Sang Kun Lee

Seoul National University Hospital, Seoul, South Korea

Purpose: To determine whether the treatment with high-dose oral diazepam could control dyskinesia in anti-NMDA receptor encephalitis, we analyzed therapeutic efficacy of high-dose diazepam in dyskinesia associated with anti-NMDA receptor encephalitis.

Methods: We reviewed the cohort data of patients diagnosed with anti-NMDA receptor encephalitis who were admitted to Seoul National University Hospital between January 2012 and July 2018 with moderate to severe dyskinesia. Diazepam was administered orally or via a nasogastric tube, 3 to 6 times a day. We assessed the treatment effect by comparing dyskinesia severity using a grading system at the initiation of diazepam treatment, on the first day of high-dose diazepam, and after one week of treatment with high-dose diazepam.

Results: Thirty-three patients with anti-NMDA receptor encephalitis and dyskinesia were treated with high-dose oral diazepam (ranging from 6 mg to 180 mg), along with immunotherapy. The severity of dyskinesia improved significantly (p -value<0.001), from median grade 3.5 (ranging from 2 to 4) to median grade 2 (ranging from 0 to

4), after one week of high-dose diazepam. No patients had serious adverse events except mild sedation.

Conclusions: We have treated the dyskinesia with high-dose oral diazepam in number of cases, and the treatment was effective and safe. This study suggests that oral administration of high-dose diazepam could be a promising treatment option for the management of severe dyskinesia in anti-NMDA receptor encephalitis.

P51

Assessment of antiseizure and neuroprotective effects of novel compounds in a delayed-treatment rat model of organophosphate (OP) exposure

Jay Spampinato, Melissa Smolik, F. Edward Dudek

University of Utah, Salt Lake City, United States

Background: It is well-known that exposure to organophosphates (OP), including nerve agents, results in status epilepticus (SE) and neuronal damage in the brain. Early control of seizure activity reduces mortality and damage. In the event of a mass release, treatment is likely to be greatly delayed compared to what would occur in a hospital setting. Therefore, there is a pressing need for treatments that can be administered after a significant delay and in a pre-hospital situation. The CounterACT Neurotherapeutic Screening (CNS) Program has now tested 9 externally submitted and 8 internally chosen compounds for this purpose.

Methods: Male, Sprague Dawley rats (150-200 g) were implanted for electroencephalogram (EEG) recordings. SE was induced by diisopropyl fluorophosphate (DFP). One hour after SE onset, rats were co-administered midazolam (MDZ) and a test compound or MDZ alone. EEG was recorded for 24 hr, followed by perfusion, tissue collection and labeling with Fluoro-Jade B. Neurons positive for Fluoro-Jade B were counted in 10 brain regions: dorsal CA1, dorsal CA3, hilus, ventral CA1, ventral CA3, amygdala, thalamus, and the parietal, entorhinal and piriform cortices. All data were analyzed quantitatively with blind procedures.

Results: Of the externally submitted compounds, compared to MDZ alone, significant anti-seizure effects were found for two compounds. These compounds reduced both seizure power and seizure duration. Each of these compounds also reduced neuronal death, compared to when MDZ was administered alone. In the same protocol, these data were compared to: (1) ganaxolone (with MDZ), which had a minimal effect on seizures, and (2) bumetanide (also with

MDZ), which had no effect on seizures. Both of these latter compounds also had no effect on neuronal death.

Conclusions: These data demonstrate that MDZ-induced suppression of OP-mediated SE can be enhanced by co-administration of other compounds, even when both compounds are administered at a long-delay (i.e., 1 hr) after SE onset. Furthermore, this delayed treatment can significantly reduce neuronal death. This screening program will continue to search for other compounds that may provide better treatment of OP-induced SE.

P52

Development of Antiepileptic Drugs Box for Status Epilepticus Fast Track (SE BOX)

Sunee Lertsinudom^{1,4}, Phiangkwan Nakornratanachai², Nanthaphan Chainirun^{2,4}, Somsak Tiamkao^{3,4}, Ratchadaporn Soontornpas²

¹Division of Pharmaceutical Care, Faculty of Pharmaceutical Sciences, Khon Kaen University, Khon Kaen, Thailand, ²Department of Pharmacy Service, Srinagarind Hospital, Faculty Of Medicine, Khon Kaen University, Khon Kaen, Thailand, ³Division of Neurology, Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand, ⁴Integrated Epilepsy Research Group, Khon Kaen University, Khon Kaen, Thailand

Background and Objective: Status epilepticus (SE) is one the most concerned issue in patient treatment. Due to it can lead to disability and mortality. Hence, the most important key is to control the seizure within 1 hour after patient had symptom. The principle of SE treatment is to shorten the time to receive the treatment. Physician must be able to give an early diagnose (Time to diagnosis) and start medicine immediately (Time to Treatment). This study aims to root cause analysis SE service problems and development SE BOX for ready to use.

Methods: The study design was action research phase I, we root cause analysis about problems of SE service by collected data from electronic hospital database between 1st October 2017 and 30st September 2018 at Srinagarind hospital.

Results: The important problems of SE service from root cause analysis 19 patients with SE were delay of treatment such as the mean time to diagnosis was 272 minutes (0-53 hours) and mean time to treatment was 32 minutes (0-80 minutes). The average waiting time of stat dose was 13.24 minutes and the percent achievement of 20 minutes guarantee time was 82.6%. However, this waiting time was collected only in pharmacy department not include the delivery time to carry the medicine to wards. Moreover, from drug information service data there were 17

questions about IV antiepileptic drug which were asked by physicians and nurse the most stability/compatibility, dose/administration, ADR/side effect respectively. From those issues, there are many steps and these can lead to the delay of treatment. As a result, Integrated Epilepsy Research Group is developing the system of antiepileptic drugs to be ready-to-use by preparing SE Box. The box consists of 4 drugs; Phenytoin injection (6 vials), Phenobarbital injection (5 amp), Sodium valproate injection (6 vials) and Levetiracetam injection (8 vials) encloses with all drug information sheets to serve information which health care provider need before drug administration.

Conclusion: SE BOX may be suitable for resolve the problems of SE service to reduce the waiting time and improve effectiveness of SE treatment; however the benefit of SE BOX need more study.

Keywords: status epilepticus; SE, AED,

P53

Intranasal midazolam as initial in-hospital treatment for status epilepticus: A pharmaco-EEG cohort study

Lara Kay^{1,2}, Nina Merkel^{1,2}, Anemone von Blomberg^{1,2}, Laurent Maximilian Willems^{1,2}, Philipp Sebastian Reif^{1,2}, Susanne Schubert-Bast^{1,2,3}, Felix Rosenow^{1,2}, Adam Strzelczyk^{1,2}

¹Epilepsy Center Frankfurt Rhine-Main and Department of Neurology, Goethe-University, Frankfurt am Main, Deutschland, ²LOEWE Center for Personalized Translational Epilepsy Research (CePTER), Goethe-University, Frankfurt am Main, Deutschland, ³Department of Neuropediatrics, Goethe-University, Frankfurt am Main, Deutschland

Background: To evaluate the efficacy and tolerability of intranasal midazolam (in-MDZ) as first line in-hospital therapy in patients with status epilepticus (SE) during continuous EEG recording.

Methods: Medical records of all patients treated with in-MDZ during EEG recording between August 2015 and April 2018 were retrospectively reviewed. Data on medical history, etiology and semiology of SE, as well as anticonvulsive medication, efficacy, and safety of in-MDZ was collected. Time to end of SE regarding administration of in-MDZ and beta-band effects were independently analysed by two board certified epileptologists on EEG and with frequency analysis.

Results: In total, 42 patients (mean age 52.7 ± 22.7 years; 23 female) were treated with a median dose of 5 mg in-MDZ (range 2.5-15 mg, mean 6.4 mg, SD 2.6) for SE. Most of the patients suffered from non-convulsive status

epilepticus (n=24; 55.8%). In total, 24 (57.1%) patients were responders as SE stopped after administering in-MDZ without any other drug being given in-between. On average, SE ceased on EEG five minutes and five seconds after application of in-MDZ (median 04:56 mins; range 00:29 mins -14:53 mins; SD 03:13mins). Frequency analysis showed an increased beta-band on EEG after application of in-MDZ at four minutes and seven seconds on average (median 03:50; range 02:20 - 05:40; SD 01:09 mins). Adverse events were recorded in six patients (14.3%) with nasal irritations in five (11.9%) and prolonged sedation in one (2.6%) patient.

Conclusions: This pharmaco-EEG based study showed that in-MDZ is effective and well-tolerated for initial treatment of SE. EEG and clinical effects occur within 04:07 and 5:05 mins on average. Intranasal administration of midazolam appears to be an easily applicable and rapidly effective alternative to buccal and intramuscular application as first line treatment if an intravenous route is not available.

P54

Effect of ZX008 (Fenfluramine HCl Oral Solution) on Total Seizures in Dravet Syndrome

Helen Cross¹, Sameer Zuberi², Iyer Anand³, Philip Sunny⁴, Elaine Hughes⁵, Archana Desurkar⁶, Kate Riney⁷, Gill Deepak⁸, Ingrid E Scheffer⁹, Lieven Lagae¹⁰, Arun Mistry¹¹, Brad Galer¹¹, Glenn Morrison¹¹, Arnold Gammaitoni¹¹, Gail Farfel¹¹, Kristin Pagano¹¹

¹UCL Great Ormond Street Institute of Child Health and Great Ormond Street Hospital, , United Kingdom, ²The Paediatric Neurosciences Group, Royal Hospital for Children, Glasgow, United Kingdom, ³Department of Neurology, Alder Hey Children's Hospital, Liverpool, United Kingdom, ⁴Neurology Department, Birmingham Children's Hospital, Birmingham, United Kingdom, ⁵Department of Paediatric Neurology, Evelina Children's Hospital, London, United Kingdom, ⁶Sheffield Children's Hospital, Sheffield, United Kingdom, ⁷Lady Cilento Children's Hospital, Brisbane, Australia, ⁸Westmead Children's Hospital, Sydney, Australia, ⁹University of Melbourne, Austin Health and Royal Children's Hospital, Melbourne, Australia, ¹⁰University of Leuven, Leuven, Belgium, ¹¹Zogenix International Limited, Berkshire, United Kingdom

Objective: Assess ZX008 (fenfluramine) effect on total seizure frequency in patients with Dravet syndrome.

Background: Dravet syndrome (DS) is a rare, severe, treatment-resistant, developmental epileptic encephalopathy. In a Phase 3, randomised, double-blind,

placebo-controlled trial, ZX008 significantly reduced convulsive seizure (CS) frequency (defined as tonic-clonic, hemiclonic, tonic, atonic, clonic, and focal motor seizures). We present secondary analyses of total seizure (TS) frequency (defined as CS plus absence or atypical absence, myoclonic, atonic, and focal seizures without clear observable motor signs).

Methods: Patients (2-18y) with DS, and CSs not controlled by current anti-epileptic drug regimen were enrolled. Following a 6-week baseline period, patients were randomised 1:1:1 to placebo, ZX008 0.2 mg/kg/day (ZX008/0.2), or ZX008 0.8 mg/kg/day (ZX008/0.8; maximum 30 mg/day), and treated for 14 weeks, including 2-week titration. Caregivers recorded seizure number and type daily via electronic diary.

Results: A total 119 patients were randomised (10.1% UK, mean age 9±4.7y). Baseline median monthly TS frequency ranged from 40.7–53.9 across groups. ZX008 significantly reduced TS frequency in a dose-related manner during 14 weeks' treatment. Median TS frequency reductions were 13.1% with placebo, 34.3% with ZX008/0.2 (p=0.031), and 70.1% with ZX008/0.8 (p<0.001). Median non-CS seizure subtype reductions (combined) were 55.6% with placebo and 75.1% with ZX008/0.8 (p<0.035), including a 54.8 and 78.6% reduction in absence and 34.8 and 64.0% reduction in myoclonic seizures, respectively. Seizure freedom was experienced by 3 (7.5%) subjects with ZX008/0.8, 3 (7.7%) with ZX008/0.2, and none with placebo. Median longest seizure-free interval was significantly longer in ZX008 groups vs placebo. ZX008 was generally well-tolerated, and no cases of FDA-defined cardiac valvulopathy were observed; neither were there echocardiographic findings or clinical symptoms suggesting pulmonary hypertension.

Conclusions: In addition to significantly reducing convulsive seizures, ZX008/0.8 mg/kg/day also significantly reduced other seizure types and Total seizure burden. ZX008 may represent an effective new treatment option for Dravet syndrome.

P55

Fenfluramine HCl Provides Long-Term Clinically Meaningful Reduction in Seizure Frequency: Results of an Open-Label Extension Study

Sameer Zuberi¹, Helen J Cross², Philip Sunny³, Anand Iyer⁴, Gail Farfel⁵, Bradley Galer⁵, Arun Mistry⁵, Lieven Lagae⁶

¹Paediatric Neurosciences Research Group, Royal Hospital for Children Glasgow, Glasgow, United Kingdom, ²UCL Great Ormond Street Institute of Child Health and Great Ormond Street Hospital, London, United Kingdom, ³Birmingham Women's and Children's Hospital, Birmingham, United Kingdom, ⁴Alder Hey Hospital, Liverpool, United Kingdom, ⁵Zogenix, Inc., Emeryville, CA, United States, ⁶Department of Paediatric Neurology, University of Leuven, Leuven, Belgium

Introduction: Fenfluramine (FFA) has demonstrated superior efficacy compared to placebo for the reduction in frequency of convulsive seizures in children and young adults (2-18 years old) with Dravet syndrome in two recently completed Phase 3 clinical trials. Here we report the preliminary interim analysis of the effectiveness and tolerability of FFA in a long-term open label extension study.

Methods: Dravet syndrome patients completing one of the Phase 3 clinical trials were eligible to enroll in the open-label extension (OLE) study. All patients entering the OLE initiated FFA at a dose of 0.2 mg/kg/day regardless of what dose they were receiving in the core trial. After 4 weeks, the dose could be titrated up in 0.2 mg/kg/day increments up to a maximum of 0.8 mg/kg/day (max 30 mg/day; 0.5 mg/kg/day [max 20 mg/day] if patient was also on stiripentol). Effectiveness and safety were assessed at months 1, 2, and 3 and then 3-month intervals thereafter.

Results: A total of 232 patients have enrolled in the study as of March 13, 2018. A total of 128 (55.2%) were male, and the mean±SD age was 9.1±4.7 years. A total of 22 (9.5%) patients discontinued treatment: lack of efficacy (16), subject withdrawal (2), adverse event (1), death (1, SUDEP), physician decision (1), and withdrawal by caregiver (1). Median duration of treatment with FFA was 256 days (range, 58-634 days). The median percent reduction in monthly convulsive seizure frequency over the entire OLE treatment period as compared with the baseline frequency established in the core Phase 3 studies was 66.8%. A clinically meaningful reduction in convulsive seizure frequency was noted at the first observation (month 1) during OLE and continued over time (Figure). Over the entire observation period, 64.4% of patients demonstrated a 50% reduction in convulsive seizure frequency and 41.2%

demonstrated a 75% reduction. At 12 months 70.4% of caregivers and 77.8% of investigators rated patients as "much improved" or "very much improved." The most common non-cardiovascular adverse events occurring in ≥10% of patients were pyrexia (21.6%), nasopharyngitis (19.4%), decreased appetite (15.9%), influenza (11.6%), diarrhoea (10.8%), and upper respiratory infection (10.3%). No patient showed echocardiographic or clinical signs of cardiac valvular heart disease or pulmonary hypertension at any time.

Conclusions: These preliminary OLE study results demonstrate FFA to provide clinically meaningful and substantial reductions in convulsive seizure frequency over time; while generally well tolerated. FFA represents a novel, highly effective antiepileptic treatment option for DS patients.

P56

Long-Term Cardiovascular Safety of Fenfluramine HCl in the Treatment of Dravet Syndrome: Interim Analysis of an Open-Label Safety Extension Study

Lieven Lagae¹, Rima Nabbout², Milka Pringsheim³, Constance Beyler⁴, Guiti Milani⁵, Juan Kaski⁶, Helen J Cross⁷, Tilman Polster⁸, Marina Nikanorova⁹, Klaus Juul¹⁰, Federico Vigeveno¹¹, Marcello Chinali¹¹, Ingrid E Scheffer¹², Gail Farfel¹³, Bradley Galer¹³, Glenn Morrison¹³, Arun Mistry¹³, Arnold Gammaitoni¹³

¹Department of Paediatric Neurology, University of Leuven, Leuven, Belgium, ²Centre de référence épilepsies rares (CReER), Paris, France, ³Paediatric Cardiology Department, German Heart Centre Munich, Munich, Germany, ⁴Paediatric Cardiology Department, Robert Debré Hospital, Paris, France, ⁵Paediatric Cardiology Department, Necker Enfants Malades Hospital, Paris, France, ⁶Great Ormond Street Hospital & UCL Institute of Cardiovascular Science, London, United Kingdom, ⁷UCL Great Ormond Street Institute of Child Health and Great Ormond Street Hospital, London, United Kingdom, ⁸Paediatric Epileptology, Krankenhaus Mara, Epilepsy Centre Bethel, Bielefeld, Germany, ⁹Danish Epilepsy Centre: Dianalund, Dianalund, Denmark, ¹⁰Paediatric Cardiology Department, Rigshospital, Copenhagen University Hospital, Copenhagen, Denmark, ¹¹Bambino Gesù Children's Hospital, Rome, Italy, ¹²University of Melbourne, Austin Health and Royal Children's Hospital, Melbourne, Australia, ¹³Zogenix, Inc., Emeryville, CA, United States

Introduction: In two recently completed Phase 3 clinical trials, fenfluramine (FFA) has demonstrated superior efficacy vs placebo for convulsive seizure reduction in

children and young adults (2-18 years old) with Dravet syndrome (DS). FFA, previously marketed for weight loss, was withdrawn from the market in 1997 following reports of cardiac valvular heart disease (VHD) and pulmonary hypertension in obese adults treated with ≥ 60 mg/day. Here we report the cardiovascular safety findings from an interim analysis of the long-term safety extension study of low-dose FFA for DS in children and young adults.

Methods: Patients with DS who successfully completed a Phase 3 study were eligible for this open-label extension (OLE) study. Patients with current cardiac VHD, pulmonary arterial hypertension, or any degree of aortic or mitral valve regurgitation were excluded from the Phase 3 trials. All patients in the OLE were started on FFA at 0.2 mg/kg/day, after 4 weeks the dose could be titrated 0.2 mg/kg/day every 2 weeks based on effectiveness and tolerability to 0.8 mg/kg/day to maximum 30 mg/day (0.5 mg/kg/day and 20 mg/day if they were taking concurrent stiripentol). Echocardiography was performed at extension study baseline, Week 6, and 3 monthly thereafter to assess cardiac valve function and pulmonary artery pressure. Cardiac VHD was defined as presence of \geq moderate mitral regurgitation and/or \geq mild aortic regurgitation. Pulmonary hypertension was considered present when pulmonary artery systolic pressure exceeded 35 mmHg.

Results: 232 patients enrolled in the study as of cut off at March 13, 2018 and received \geq one dose of FFA, (9.5%) patients have discontinued treatment due to: lack of efficacy (16), subject withdrawal (2), adverse event (1), death (1, SUDEP), physician decision (1), or withdrawal by caregiver (1). Demographics include 128 (55.2%) male patients, mean \pm SD age of 9.1 \pm 4.7 years. The median FFA treatment duration was 256 days (58-634 days). No patient demonstrated cardiac VHD or pulmonary arterial hypertension during the study. The most common finding was intermittent and transient physiologic/trace valve regurgitation, also seen in normal healthy children and young adults.

Conclusions: The results of this long-term safety study demonstrate no development of cardiac VHD or pulmonary hypertension after daily treatment with FFA for \leq 21 months in DS patients. Together with the efficacy data from the Phase 3 trials, fenfluramine appears to have a positive benefit-risk profile in this patient population.

P57

A Study of Trends of Intravenous Antiepileptic Drugs in Patients with Status Epilepticus

Somsak Tiamkao^{1,4}, Panisa Manasirisuk², Nanthaphan Chainirun², Sunee Lertsinudom³, Ratchadaporn Soontornpas²

¹Division of Neurology, Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand,

²Department of Pharmacy Service, Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand,

³Division of Pharmaceutical Care, Faculty of Pharmaceutical Sciences, Khon Kaen University, Khon Kaen, Thailand, ⁴Integrated Epilepsy Research Group, Khon Kaen University, Khon Kaen, Thailand

Background and Objective: Status epilepticus (SE) called the neurological emergency. Currently, we have many kinds of intravenous antiepileptic drugs (AEDs) despite conventional antiepileptic drugs and new antiepileptic drugs. Therefore, objective of this study is acquiring for trends and cumulative cost of intravenous AEDs in patients with SE.

Methods: The study was a descriptive, retrospective study. Data from electronic hospital database were collected between 1st October 2015 to 30st September 2018 (financial year 2016 to 2018) in patients with SE who received intravenous AEDs (conventional AEDs; phenytoin, sodium valproate, phenobarbital and newer AEDs; levetiracetam) at Srinagarind hospital.

Results: The results showed that 190 SE patients (93 men and 97 women) whose mean age 39.14 years \pm 24.24. Convulsive status epilepticus was most common (294 events, 98%) vs non-convulsive status epilepticus (6 events, 2%). Consideration of hospital admission rate of conventional AEDs, we found phenytoin and phenobarbital were decreased (phenytoin; 39.20% in 2016, 36.64% in 2017, 33.60% in 2018 and phenobarbital 14.86% in 2016, 14.85% in 2017, 5.60% in 2018) and sodium valproate was increased in 2018 (14.86% in 2016, 13.86% in 2017, 16.80% in 2018). If considerate proportions of hospital admission rate who received each type of intravenous AEDs between conventional AEDs and newer AEDs were associated with a decreased rate of conventional AEDs used (conventional AEDs; 68.92% in 2016, 65.35% in 2017, 56.00% in 2018 and newer AEDs; 31.08% in 2016, 34.65% in 2017, 44.00% in 2018). Moreover, proportions of first-line treatment of intravenous AEDs were increased in newer AEDs (28.57% in 2016, 30.00% in 2017 and 47.78% in 2018; 19.21% increasing).

Conclusion: Trends of newer AEDs used were increased, it appears that trends of intravenous AEDs used were changed. This study will be a useful basic information for evaluate pharmacy purchasing system and drug use evaluation.

Keywords: trends, intravenous antiepileptic drugs

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Intravenous antiepileptic drugs in adults with benzodiazepine-resistant convulsive status epilepticus: a systematic review and network meta-analysis

Francesco Brigo^{1,2}, Cinzia Del Giovane³, Eugen Trinka⁴, Simona Lattanzi⁵

¹Franz Tappeiner Hospital, Merano, Italy, ²University of Verona, Verona, Italy, ³University of Bern, Bern, Switzerland, ⁴Paracelsus Medical University, Salzburg, Austria, ⁵Marche Polytechnic University, Ancona, Italy

Background: The aim of this study was to estimate the comparative efficacy and tolerability of antiepileptic drugs (AEDs) in benzodiazepine-resistant convulsive status epilepticus (SE).

Methods: MEDLINE, CENTRAL, ClinicalTrials.gov and Opengrey.eu were searched for randomized controlled trials (RCTs) of AEDs used intravenously to treat benzodiazepine-resistant SE in adults. The outcomes were: total initial control of SE; seizure freedom at 24 hours without SE recurrence; respiratory depression; hypotension. Effect sizes were estimated as odds ratios (ORs) with their 95% confidence intervals (CIs) using pairwise and network meta-analyses. The hierarchy of competing interventions was established using the surface under the cumulative ranking curve (SUCRA) and mean ranks.

Results: Five RCTs were considered, involving 459 patients. Included interventions were valproate (VPA; 20-30 mg/kg), phenytoin (PHT; 20 mg/kg), diazepam (DZP; 0.2 mg/kg, then 4 mg/h), phenobarbital (PB; 20 mg/kg, then 100 mg every 6h), lacosamide (LCM; 400 mg) and levetiracetam (LEV; 20 mg/kg). Total initial control of SE was significantly higher with LEV compared to PHT (OR 21.77; 95% CI: 1.16-409.79), and with PB compared to PHT (OR 7.48; 95% CI 1.59-35.32) and VPA (OR 5.36; 95% CI 1.87-15.36). Seizure freedom at 24 hours was significantly higher with PB compared to VPA, DZP, and LCM. There were no statistical differences across treatments in the incidence of respiratory depression; hypotension was less common with VPA than PHT. According to SUCRA, LEV and PB had the greatest probabilities of being best in the achievement of initial SE control and seizure freedom, respectively. VPA and LCS had the greatest likelihood ranking best while PB and PHT ranking worst for tolerability.

Conclusions: High-dose PB resulted highly effective in controlling SE and preventing seizure recurrence, but less well tolerated. LEV was associated with high rate of initial

SE control, but did not appear to effectively prevent SE recurrence. LCM and VPA were less effective, but better tolerated than PB. Further head-to-head comparative studies are strongly required to provide more definitive evidence. The Established Status Epilepticus Treatment Trial (ESETT) is the larger ongoing trial aimed to compare fosPHT, VPA and LEV in benzodiazepine-resistant SE.

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Cost and Expense of Intravenous Levetiracetam for Treatment of Acute Seizure in Tertiary Hospital in Thailand

Sunee Lertsinudom^{1,4}, Sirin Phenphinan¹, Anyamanee Lapmag², Somsak Tiamkao^{3,4}

¹Clinical Pharmacy Division, Faculty Of Pharmaceutical Sciences, Khon Kaen University, Khon Kaen, Thailand, ²Division of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Ubon Ratchathani University, Ubon Ratchathani, Thailand, ³Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand, ⁴Integrated Epilepsy Research Group, Khon Kaen University, Khon Kaen, Thailand

Background: Epilepsy is a chronic condition that required long-term treatment with antiepileptic agents. Levetiracetam is the new generation antiepileptic agent which is commonly used for treatment of various type of seizure, as well as status epilepticus. The costs of treatment are very impact on patients with epilepsy and health system. The availability of an intravenous preparation is advantage, but with the high price, intravenous levetiracetam treatment tends to be more expensive than conventional treatments. This study aimed to describe the cost and expense of intravenous levetiracetam used to control symptoms in patients with acute seizure.

Methods: A retrospective descriptive study conducted at Khon Kaen University Hospital in Thailand. Patients over 15 years old who had diagnosed as acute seizure and had received intravenous levetiracetam treatment between January 1, 2010 and December 31, 2014 were enrolled into the study. The cost of levetiracetam used and the expense of treatment that the patients had to pay for control seizure were determined. Data of all eligible patients were analyzed by descriptive statistics. The cost and expense of intravenous levetiracetam treatment are expressed in term of median and interquartile range (IQR).

Results: During the study period, 332 patients with acute seizure receiving intravenous levetiracetam were included. Among these patients, 91 were status epilepticus and 241

were non-status epilepticus. The average age of patients was 55.7 (20.4) years with equal sex distribution. Most patients received intravenous levetiracetam for loading dose of 1,000 mg (167 patients: 50.3%) and maintenance dose of 1,000 mg/day (254 patients: 76.5%), respectively. The median cost of intravenous levetiracetam used per admission for patients with acute seizure was 9,095 THB (363.8 USD). From the patient's perspective, the median total expense per admission was 162,609 THB (6,504.4 USD), which was due to the expense for intravenous levetiracetam 12,384 THB (495.4 USD)

Conclusions: The expense for intravenous levetiracetam was only 7.6% of total expense per admission. Although the expense for intravenous levetiracetam treatment is low, however, further analyses are required to investigate the cost-effectiveness of intravenous levetiracetam in patients with acute seizure.

Keywords: levetiracetam, acute seizure, cost, expense

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Clinical outcome of intravenous Levetiracetam in acute seizure, Tertiary care hospital, Thailand

Sunee Lertsinudom^{1,3}, Somsak Tiamkao^{2,3}, Anyamanee Lapmag¹

¹Faculty of Pharmaceutical Science, Khon Kaen University, Khon Kaen, Thailand, ²Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand, ³Integrated Epilepsy Research Group, Khon Kaen University, Khon Kaen, Thailand

Background: Intravenous levetiracetam has been approved for use as an antiepileptic drug, as well as in cases of acute seizure. There are few reports that detail the clinical data and outcomes in seizure control within 30 minute and seizure control which categorized by treatment order of intravenous levetiracetam.

Method: This was a retrospective analytical study conducted at Khon Kaen University's Srinagarind Hospital in Thailand. The study period was between January 1, 2010 and December 31, 2014. The inclusion criteria were that patients were over 15 years old, had received intravenous levetiracetam treatment. The main clinical outcomes were seizure control within 30 minute and seizure control which categorized by treatment order of intravenous levetiracetam. Clinical outcomes were compared between status epilepticus and non-status epilepticus.

Results: During the study period, there were 332 patients

who met the study criteria. The average age of the patients was 55.7±20.4 years which nearly equal sex distribution. Of those, 91 patients (27.4 %) had status epilepticus and 241 patients (72.6%) had non-status epilepticus. Intravenous levetiracetam was administered as the first line (it mean after initial benzodiazepine), second line, third line and fourth line antiepileptic drug in 192 patients (57.8%), 107 patients (32.2%), 28 patients(8.4%) and 5 patients (1.5%) respectively. The seizure control rate within 30 minute after administration of intravenous levetiracetam in the status epilepticus was significant less than in the non-status epilepticus groups (49.5%, 90%; p <0.001) but number of patients who dead in status epilepticus and non-status epilepticus groups were not difference (31.9%, 33.2%; p=0.78). Seizure control rate of acute seizure patients who received intravenous levetiracetam in first line, second line, third line and fourth line were 86.9%, 81.3%, 57.1% and 20% respectively.

Conclusion: Intravenous levetiracetam was effective in acute seizure especially in first line treatment.

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Comparison of Efficacy between Original and Generic Intravenous Levetiracetam for Acute Repetitive Convulsive Seizure or Status Epilepticus

Somsak Tiamkao¹, Rachot Wongjirattikarn¹, Sineenard Pranboon², Siriporn Tiamkao³, Integrated Epilepsy Research Group⁴

¹Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand, ²Nursing Division, Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand, ³Department of Pharmacy, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand, ⁴Integrated Epilepsy Research Group, Khon Kaen University, Khon Kaen, Thailand

Background: Intravenous Levetiracetam (IV LEV) is approved for treatment status epilepticus (SE). However, owing to high drug cost, additional expenses is considered in providing medical care.

Objective: To compare the efficacy of original and generic IV LEV for acute repetitive convulsive seizure (ARCS) or SE.

Methods: Forty patients aged 18 years or older with diagnosed SE or ARCS were randomized double blind study. Patients were randomly assign in 1:1 ratio, via computer generated code, to receive original IV LEV or generic IV LEV (Focale®). The primary outcomes were the seizure control and the number of seizure exacerbations

during 24 hours after drug administration, while the secondary outcome was electroencephalographic (EEG) findings, serious adverse events and clinical outcome at hospital discharge.

Results: Forty patients were randomly assigned treatment into 20 patients (10 SE patients and 10 ARCS) taking original IV LEV and 20 patients (7 SE patients and 13 ARCS) taking generic IV LEV (Focale®). There was no significant difference in patient's baseline characteristics. The seizure control rate were 75 % in original IV LEV group, and 65 % in the Focale® group (p-value 0.490). Five (25 %) patients in original IV LEV group, and 6 (30 %) patients in the Focale® group developed seizure exacerbations within 24 hours after drug administration (p-value 0.723). The day 3 EEG outcome were positive in 2 patient taking original IV LEV, and 3 patient taking Focale® (p-value >0.326). There was not any report of drug -related adverse event. The final clinical outcome; 17 patients were improved in both groups (p=0.549). Two patients dead in original IV LEV, 1 in generic Focale® group (p>0.999).

Conclusion: Treatment with Focale® were non-inferior, compared with original IV LEV. Therefore, it might be useful alternative to original IV LEV for treatment of SE and ARCS.

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Drug use review of Intravenous Levetiracetam in Status Epilepticus patients at Srinagarind Hospital, Khon Kaen, Thailand

Supinya Tuntapakul^{1,3}, Somsak Tiamkao^{2,3}, Sunee Lertsinudom^{1,3}

¹Clinical Pharmacy Division, Faculty of Pharmaceutical Sciences, Khon Kaen University, Khon Kaen, Thailand, ²Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand, ³ Integrated Epilepsy Research Group, Khon Kaen, Khon Kaen, Thailand

Background: Intravenous levetiracetam (ivLEV) has been approved for use in cases of status epilepticus. Despite the widespread use of ivLEV, there are few reports that detail the clinical use, outcomes and adverse drug reactions (ADRs) associated with this antiepileptic drug. This study aimed to review the clinical use, outcome and ADRs of ivLEV in patients with status epilepticus.

Methods: A retrospective descriptive study. The inclusion criteria were patients with status epilepticus, age over 15 years old, received ivLEV treatment at Srinagarind Hospital, Khon Kaen University between January 2014 and December 2014.

Results: There were 53 status epilepticus patients and received ivLEV. Patients were male 29 patients (54.72%), the mean age was 57.34 years old (SD 19.82 years) and the mean weight was 58.47 Kg (SD 13.04 kg). Most common known cause status epilepticus were hypoxic ischaemic encephalopathy 12 patients (22.64%). The patients received ivLEV for first line treatment were 4 patients (7.55%), second line treatment were 36 patients (67.92%) and third line treatment were 13 patients (24.53%). The patients received ivLEV dosage between 1000 mg/day and 1500 mg/day for loading and maintenance dosage between 500 mg/day and 2000 mg/day. The seizure control and non-recurrent seizure within 24 hour after received ivLEV were 32 patients (60.38%), 20 patients (37.74%) had seizure frequency decrease more 50 % or need antiepileptic more 3 drugs for treatment and 1 patient had uncontrolled seizure. In case of seizure control, we found in patients who received ivLEV for first line treatment was 1 patient (3.13%), second line treatment were 25 patients (78.13%) and third line treatment were 6 patients (18.75%). No major ADRs, in these study 3 patients (5.66%) had minor ADRs such as rash and itching.

Conclusions: ivLEV had efficacy to controlled seizure in status epilepticus especially in second line treatment after received diazepam and had minor ADRs but the cost effectiveness study need more study.

P63

Intravenous Brivaracetam in the treatment of status epilepticus: a systematic review

Francesco Brigo^{1,2}, Simona Lattanzi³, Eugen Trinka⁴

¹Franz Tappeiner Hospital, Merano (BZ), Italy, ²University of Verona, Verona, Italy, ³Marche Polytechnic University, Ancona, Italy, ⁴Paracelsus Medical University, Ancona, Italy

Background: Brivaracetam (BRV) is a high-affinity synaptic vesicle glycoprotein 2A (SV2A) ligand. Although structurally related to levetiracetam, BRV has higher brain permeability, faster brain SV2A occupancy, and more rapid onset of action. These properties make BRV potentially an ideal compound in the emergency setting. The aim of our study was to systematically review the evidence about the clinical efficacy and tolerability of BRV in the treatment of SE.

Methods: We searched Medline, Embase, Google Scholar, and ClinicalTrials.gov (accessed from inception to December 3, 2018) to identify studies evaluating

intravenous BRV as treatment of SE of any type in patients of any age. We also searched the OpenGrey repository and conference proceedings of international congresses by the International League Against Epilepsy and by the American Epilepsy Society from 2016 to 2018.

Results: Seven studies were included, with a total of 37 patients aged 22 to 85 years (21 females). The type and etiology of SE varied remarkably across studies. The number of drugs used prior to BRV to treat SE ranged from 1 to 8. The time from SE onset to BRV administration ranged from 0.5 hour to 105 days. The initial BRV dose ranged from 50 to 400 mg. The proportion of patients achieving clinical SE cessation varied from 27% to 100%. The time from BRV administration to SE cessation ranged from 15 minutes to 94 hours. No serious adverse effects were reported.

For 6 responders in whom BRV was used as last medication individual patient data were available. In these patients (age: 61 ± 25 years; maximal median BRV dose: 200 mg, range: 100-400 mg) the median time from BRV administration to SE cessation was 15 hours (range: 15 minutes-27 hours).

Conclusions: The available data suggested that BRV has a good safety profile and rapid onset of action. The current evidence is however based only on few case reports and small case series and, hence, hampered by several confounding factors and high risk of biases. Further prospective studies in clinically homogeneous and larger cohorts are warranted to explore the potential benefit of BRV for treatment of SE.

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Experience of the use of Brivaracetam in status epilepticus (a Spanish multicentric registry)

Estevo Santamarina¹, Beatriz García Parejo², Jacint Sala³, Álvaro Gutiérrez-Viedma², Júlia Miró³, Montserrat Asensio⁴, Laura Abraira¹, Mercé Falip³, Jaime Ojeda⁵, Francisco Javier López⁶, Xiana Rodríguez⁶, José Ángel Mauri⁷, Maria Aiguabella³, Irene García-Morales², Manuel Toledo¹

¹Hospital Vall Hebron, Barcelona, Spain, ²Hospital Clínico San Carlos, Madrid, Spain, ³Hospital Universitario Bellvitge, L'Hospitalet, Barcelona, Spain, ⁴Hospital General Universitario Alicante, Alicante, Spain, ⁵Hospital Infanta Sofía, San Sebastián de los Reyes - Madrid, Spain, ⁶Hospital Clínico Universitario, Santiago de Compostela - A Coruña, Spain, ⁷Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain

Background: Pharmacokinetics of brivaracetam (BRV) added to its efficacy observed in animal models of status

epilepticus (SE), make this drug attractive for its use in emergency situations. So far, two series with few cases have been published. Our objective was to evaluate the use of intravenous BRV in a larger sample of patients.

Methods: A multicenter registry of SE cases treated with BRV administration was performed. These patients were registered between January and December 2018 in 7 hospitals in Spain. Demographic variables, SE features, concomitant drugs, load doses and efficacy were collected.

Results: A total of 43 patients were assessed. The mean age was 56 ± 23.1 years old. 51.2% were male. 29 had a previous epilepsy. 24 (55.8%) had prominent motor symptoms and 19, non-convulsive symptoms. Regarding the etiology, 19 (44.2%) were considered acute symptomatic, 16 (17.2 %) delayed symptomatic, 4 (9.3%) progressive symptomatic and 4 (9.3 %) cryptogenic. Looking at the concomitant FAEs, 17 of them had previously received Levetiracetam (LEV). In 14 patients, BRV was used early (1st-2nd antiepileptic). The median load dose was 100mg (50-400); and the dose adjusted by weight was 1.8mg / kg (0.4-7.3). The BRV was effective in 54% (23) and a response was observed <6 hours in 10 of them. We observed a tendency to be more effective when administered earlier ($p = 0.09$). In those with the fastest responses we observed that both the total administered dose (300mg vs 100mg, $p = 0.002$) and that adjusted by weight (4.5mg / kg vs. 1.25mg / kg, $p = 0.002$) were significantly higher.

Conclusion: BRV is useful in the treatment of SE, with a response rate of 53% (even with the previous taking of LEV). The response rate seems higher when it is administered earlier. The responses in the first 6 hours are observed with higher doses (300mg - 4.5mg / kg).

P65

Efficacy and Safety of Intravenous Brivaracetam as a Treatment for Increased Seizure Activity in an Epilepsy Monitoring Unit

Jerzy Szaflarski¹, Ahmed Sadek², Bernhard Greve³, Paulette Williams⁴, Julie Varner⁴, Brian Moseley⁵

¹University of Alabama at Birmingham, Birmingham, USA, ²Neurological Services of Orlando, Orlando, USA, ³UCB Pharma, Monheim am Rhein, Germany, ⁴UCB Pharma, Raleigh, USA, ⁵University of Cincinnati, Cincinnati, USA

Background: Additional treatment options are needed for acute seizures. Therefore, we assessed the efficacy and safety of intravenous (IV) brivaracetam (BRV) vs IV lorazepam (LZP) for acute seizures in patients with

epilepsy undergoing evaluation in an Epilepsy Monitoring Unit (EMU).

Methods: Phase 2, open-label, randomized, parallel-group, active-controlled proof-of-concept trial (EP0087; NCT03021018). Patients (18-70 years) admitted to EMU were randomized 1:1:1 to single-dose bolus IV LZP (dose per Investigator's practice), IV BRV 100 mg, or IV BRV 200 mg. Administration of trial medication was started by a seizure requiring intervention. Treatment period: from trial medication administration up to 12 hours or until next seizure or until rescue medication administration; safety follow-up: end of treatment period to 24 hours. Primary efficacy outcome: time to next seizure (per clinical observation with electroencephalogram confirmation) or rescue medication; secondary outcomes: time to next seizure (per clinical observation) or rescue medication, seizure freedom and rescue medication use 12 hours after end of trial medication administration; safety outcomes: treatment-emergent adverse events (TEAEs).

Results: 11/45 (24.4%) randomized patients who received trial medication for a qualifying seizure had a seizure within 12 hours (LZP=5, BRV 100 mg=3, BRV 200 mg=3), suggesting similar efficacy across treatments, consistent with Kaplan-Meier analysis. Most patients were seizure free at 12 hours: LZP 60.0%, BRV 100 mg 80.0%, BRV 200 mg 80.0%. Rescue medication use at 12 hours was numerically higher for LZP (40.0%; BRV 100 mg 6.7%, BRV 200 mg 13.3%). TEAEs were reported by 31.3%, 40.0%, 20.0% of LZP, BRV 100 mg, BRV 200 mg patients; one LZP patient (6.3%) reported a serious TEAE (seizure cluster).

Conclusions: IV LZP, IV BRV 100 mg, IV BRV 200 mg showed similar efficacy in controlling acute seizures in the EMU. TEAEs were as expected. This exploratory trial suggests a possible role of BRV in this setting.

STUDY SUPPORT: UCB Pharma-sponsored

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Multicenter cohort study on the use of topiramate in the treatment of refractory and super-refractory status epilepticus

Anne Fechner¹, Kristina Hubert¹, Kolja Jahnke¹, Susanne Knake², Jürgen Konczalla¹, Katja Menzler², Michael Ronellenfisch¹, Felix Rosenow¹, Adam Strzelczyk^{1,2}

¹Goethe-University Frankfurt, Frankfurt, Germany, ²Philipps-University Marburg, Marburg, Germany

Background: Status epilepticus (SE) represents a medical emergency and is associated with significant morbidity and mortality. With a refractory and super-refractory course of an SE the response to further anticonvulsants decreases. Topiramate (TPM) is an orally available anticonvulsant approved since 1996. A variety of mechanisms of action are attributed to TPM, including blockage of the voltage-dependent sodium and calcium channels, increased activity of GABA receptors and voltage-dependent potassium channels, influence on glutamate receptors, and inhibition of carboanhydrase. The aim of this study was to characterize and efficacy of TPM in the therapy of refractory and super-refractory SE.

Methods: All patients who received TPM for treatment of SE between 2011 and 2016 at the University Hospitals in Frankfurt and Marburg were included in this retrospective analysis. Data on the medical history, etiology and course of the SE were systematically collected, as were data on therapies performed.

Results: A total of 106 patients (67.4±18.07 years, 61 female [57.5%]) were treated with TPM. The median SE duration before TPM initiation was 8.5 days. The treatment continued in median over 11 days. The median number of previous antiepileptic drugs (AED) used was 5. Initial TPM dose ranged between 25mg and 500mg (median 100mg), titrated to a daily dose of 25 to 900mg (median 400mg). The administration of TPM occurred generally per os or via nasogastric tube. SE was controlled in 27% (29/106) of patients receiving TPM as their last drug. During the treatment of TPM one pancreatitis was noticed and we observed increased ammonia levels in 38 patients (35.9%). The intrahospital mortality was 22.6% (n=24).

Conclusions: Based on these results and published case series, TPM can be considered as another therapeutic option for the treatment of refractory SE. Larger randomized and controlled trials are needed to evaluate the efficacy of TPM in SE.

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Perampanel-induced psychiatric adverse events: Associated with Human leukocyte antigen subtypes

Hyeyeon Chang¹, Tae-Joon Kim², Yong-Won Shin¹, Jangsup Moon¹, Soon-Tae Lee¹, Kyung-Il Park¹, Kon Chu¹, Ki-Young Jung¹, Manho Kim¹, Sang Kun Lee¹

¹Seoul National University Hospital, Seoul, South Korea, ²Ajou University hospital, Suwon, Suwon

Background: Perampanel (PRP) is a new AED, selective non-competitive antagonist of AMPA receptors. The medicine has a unique mechanism of action as a -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor antagonist. This drug is effective for both partial and generalized epilepsy, has low drug interactions and well tolerated. Nevertheless, the use of PRP can be limited by some psychiatric adverse events (PAEs) that cause drug withdrawal. But the mechanism of PRP-induced PAE has not been elucidated. Here we performed human leukocyte antigen (HLA) genotyping in patients with epilepsy taking PRP and investigated PRP-induced PAE in HLA-related immunopathogenesis

Methods: 17 patients with PRP-induced PAEs were included in this study. PRP-induced PAE was diagnosed when PAE including psychosis (e.c: delusion), aggressive behavior and suicide attempt occurred during PRP administration, and the symptoms of PAE improved PRP stopped. The HLA genotype of the PRP-induced PAE group was compared with 19 patients with PRP tolerance and 485 ordinary Korean people. The PRP tolerance group consisted of patients without side effects despite taking more than 10 mg of PRP a day for at least 6 months.

Results: The genotype frequency of the HLA-DQB1 * 06: 01 allele was significantly higher in the PRP-induced PAE group compared to the general population ($p = 0.008$, OR 3.94). The frequency of the DRB1 * 08: 03 allele was significantly higher than PRP resistant group ($p = 0.037$, OR 9.24) and the general population ($p = 0.041$, OR 2.97). There, HLA-B * 54: 01 was remarkably frequent in the PRP-induced PAE group than the general population ($p = 0.041$, OR 3.25).

Conclusion: Present study is the first trial to elucidate the association between the PRP immune system HLA and PAE. These findings suggest that the HLA allele could be a risk factor for PAE induced by PRP.

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Perampanel therapeutic drug monitoring with saliva: correlation with plasma concentrations

Eun Young Kim¹, Yong-Won Shin¹, Do-Yong Kim¹, Hyeyeon Chang¹, Jangsup Moon², Soon-Tae Lee¹, Keun-Hwa Jung¹, Kyung-Il Park¹, Ki-Young Jung¹, Manho Kim¹, SeoungHwan Lee³, In-Jin Jang³, Kon Chu¹, Sang Kun Lee¹

¹Department of Neurology, Seoul National University Hospital, Seoul, South Korea, ²Department of Neurosurgery, Seoul National University Hospital, Seoul, South Korea, ³Department of Clinical Pharmacology and Therapeutics, Seoul National University Hospital, Seoul, South Korea

Background: Therapeutic drug monitoring (TDM) of antiepileptic drugs (AEDs) is an aid to optimizing the drug management of patients with epilepsy. Salivary testing is a non-invasive and easily repeatable procedure, with several other advantages. Owing to technical advances, salivary TDM has become a feasible option for the TDM of several drugs including AEDs, and its value has been investigated by previous studies. However, until recently, such studies have not been conducted for perampanel. We aimed to assess the quantifiability of perampanel concentrations in the saliva and their correlation with those of the plasma.

Methods: Adult patients with a diagnosis of epilepsy prescribed perampanel from August 2018 to October 2018 in our hospital were enrolled. Perampanel concentrations were measured from simultaneously obtained plasma and saliva samples. We analyzed the correlation of concentrations of perampanel in plasma and saliva.

Results: Seventeen patients were enrolled in this study. Their ages ranged 16 to 57 (median 30), and 7 (41%) were women. Patients were on 4 to 12 mg of perampanel, and samples were obtained between 12 hours to 39 hours (median 15 hours) after the intake of the last dose of perampanel. Median plasma and salivary concentration of perampanel were 254.5 (1.55-883.0) and 4.68 (0.25-22.1), respectively. There was a close linear relationship between perampanel concentrations in plasma and saliva, with a high correlation coefficient ($r = 0.941$, $p = < 0.001$).

Conclusions: Perampanel concentration in saliva is highly correlated with that of plasma. Our results demonstrate that perampanel is measurable in saliva and has therapeutic potential in the application of its TDM.

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Clinical Characteristics of Excellent Responder of Perampanel in Epilepsy

Hye-Rim Shin, Jangsup Moon, Kon Chu, Sang Kun Lee

Seoul National University Hospital, Seoul, South Korea

Background: Perampanel (Fycompa) is newly developed anti-epileptic drug (AED) which targets AMPA (alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) receptor. Since perampanel has different mechanism from previous AEDs, such as sodium channel blocker, and GABA-related drugs, it is expected to have clinical efficacy in many drug-refractory seizures. However, we cannot predict whether the individual patient would be good responder to the drug. So in this study, we aimed to investigate the clinical characteristics of excellent responders to perampanel .

Methods: We reviewed patient's characteristics, and combined treatment of epilepsy patients who started perampanel between April 2016 to March 2018. Effect of the perampanel was evaluated 6 months after the drug was started. The excellent responder of perampanel was defined as who achieved free of generalized tonic clonic seizure (GTCS), or more than 50% reduction of non- GTCS.

Results: Total 219 patients were reviewed, and the excellent responder was 12 patients. The average age of excellent responder was younger (average 33.5 years) than non-responder (average 39.0 years), and 7 patients (58.3%) were male. In excellent responder, 5 patients had generalized, and 7 patients had focal epilepsy. Seizure semiology also included various kinds of seizures, such as GTCS, atonic, or simple partial seizures. The number of other AEDs combined with perampanel was median 3 (range 2 - 5), and most common AEDs combined with perampanel was levetiracetam (9 patients), and valproic acid (8 patients). The final dose of perampanel was median 6mg (range 4 - 10mg).

Conclusions: We found excellent responder of perampanel after 6 month of treatment with perampanel. We should collect more data of clinical, and genetic characteristics of the excellent responder, to find what characteristics could predict the excellent responder of perampanel.

P70

Efficacy and safety of intravenous lacosamide in paediatric status epilepticus: a single centre experience

Sara Matricardi¹, Sabrina Siliquini¹, Elisabetta Cesaroni¹, Ida Cursio^{1,2}, Silvia Cappanera¹, Liliana Porfiri¹, Nelia Zamponi¹

¹Department of Neuropsychiatry, Children's Hospital "G. Salesi", Ospedali Riuniti, Ancona, Italy, ²Child and Adolescent Neuropsychiatry Unit, University of Cagliari, Cagliari, Italy

Background: Lacosamide (LCM) is a third-generation antiepileptic drug (AED) with a unique mechanism of action approved as a monotherapy or adjunctive therapy in patients older than 4 years of age with focal seizures, with or without secondarily generalization. LCM has been reported to be effective in adult status epilepticus (SE), but data of its effectiveness in paediatric SE are still scanty. The aim of this study was to assess the efficacy and safety of intravenous (iv) LCM in the treatment of SE in a cohort of paediatric patients.

Methods: We performed a retrospective observational cohort study, enrolling paediatric patients who received at least one dose of iv LCM for SE from April 2010 to December 2018.

All clinical and treatment data were reviewed and analysed. Efficacy was defined as cessation of seizures or significant (> 50%) reduction in seizure frequency. Treatment emergent adverse events were recorded.

Results: The series comprised 22 patients with a median age at SE onset of 10 years old (interquartile range [IQR]: 7-12 years). Eighteen (81%) patients had previous history of drug resistant epilepsy and received a median of 3 AEDs. All patients had established or refractory SE. The aetiology was: structural (36.3%), unknown (27.2%), genetic (22.7%), and immune (13.6%). Prior to iv LCM administration, conventional AEDs for SE were used, including midazolam, phenobarbital, levetiracetam, valproate; LCM was used as the third or fourth treatment. The median loading dose of LCM was 6.7 mg/kg (IQR: 4.5-8.6 mg/kg). The use of LCM was associated with resolution of SE in 54.5%. No significant treatment emergent adverse events and drug interactions were recorded during and for 48 h following the iv LCM administration, only 1 patient had transitory bradycardia without prolongation of the PR interval.

Conclusions: Intravenous LCM is a promising agent in the management of SE in children and a good alternative to

standard AEDs. The favourable safety profile could also allow an earlier use in the treatment regimen.

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Allopregnanolone Pharmacokinetic Pharmacodynamic Modeling and Simulations in Dogs with Naturally-Occurring Epilepsy

Irene Vuu^{1,2}, Edward Patterson³, Chun-Yi Wu⁴, Dorota Zolkowska⁴, Ilo Leppik^{1,5}, Michael Rogawski⁴, Gregory Worrell⁶, Vaclav Kremen^{6,7}, James Cloyd^{1,2}, Lisa Coles^{1,2}

¹Department of Experimental and Clinical Pharmacology, University of Minnesota College of Pharmacy, Saint Paul, United States, ²Center for Orphan Drug Research, University of Minnesota College of Pharmacy, Minneapolis, United States, ³University of Minnesota College of Veterinary Medicine, Saint Paul, United States, ⁴Department of Neurology, University of California Davis School of Medicine, Sacramento, United States, ⁵UMP MINCEP Epilepsy Care, Minneapolis, United States, ⁶Department of Neurology, Mayo Clinic, Rochester, United States, ⁷Czech Institute of Informatics, Robotics, and Cybernetics, Czech Technical University, Prague, Czech Republic

Allopregnanolone (ALLO), a neurosteroid that positively modulates synaptic and extrasynaptic GABA_A receptors, may be useful as a first-line treatment for human and canine status epilepticus (SE). We completed an IV and IM ALLO pharmacokinetic-pharmacodynamic (PKPD) study in dogs. The objectives of this work were: 1) build a PKPD model relating plasma ALLO concentrations to electroencephalographic (EEG) activity, and 2) simulate EEG effects of IV and IM ALLO doses.

Three healthy dogs and two with epilepsy and implanted intracranial electrodes were used. ALLO doses ranging from 1-6 mg/kg were infused IV over 5 minutes in five dogs or injected IM in two dogs. EEG data were collected across three IV doses (1-3 mg/kg). Blood samples were collected up to 6 hrs post-dose. ALLO concentrations were measured by a UPLC-MS/MS system. PKPD modeling and simulation were performed using Phoenix NLME (version 8.0). EEG were analyzed using Matlab (version 2018b). A PK model was developed to describe IV/IM administration simultaneously. Thereafter, PK parameter estimates were fixed and Emax indirect-link PD models were evaluated.

ALLO exhibits dose-proportional, two-compartment PK at the doses studied (V_1 : 6.3 L/kg, V_2 : 23 L/kg, CL_1 : 128 L/hr/kg, CL_2 : 34.2 L/hr/kg, IM absorption rate constant: 1.0 1/hr, bioavailability: 69%). Concentration-EEG data were best fit by sigmoidal Emax models (Δ - k_{e0} : 1-1.5 1/

min, EC_{50} : 651-700 ng/mL; THETA - k_{e0} : 0.5-1.31 1/min, EC_{50} : 397-672 ng/mL; ALPHA - k_{e0} : 0.3-1.24 1/min, EC_{50} : 161-699 ng/mL; and BETA - k_{e0} : 0.26-0.75 1/min, EC_{50} : 150-200 ng/mL). The effect was rapid (k_{e0} half-life of 1-2.7 minutes) across all frequency bands. The beta frequency band showed an increase in power density at the lowest concentrations compared to the others. Simulations show that maximum effect would be attained 30 seconds after IV infusion and 10 minutes after IM injection, and effect duration lengthened in a dose-dependent manner.

In conclusion, IV ALLO results in rapid EEG changes. The increase in beta frequency band power density is comparable to published EEG changes associated with benzodiazepines. Simulations suggest IM ALLO has an onset of effect similar to that of IM midazolam. Our results support further evaluation of ALLO for SE in dogs and humans.

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Utility of ketamine in super-refractory status epilepticus in children- Experience in a tertiary centre in Hong Kong

Eva Fung, Maggie Yau, Kwan Ming Yam

The Chinese University Of Hong Kong/ Prince Of Wales Hospital, Shatin, Hong Kong

Background: Super-refractory status epilepticus (SRSE) is a medical emergency that treatment itself may be associated with morbidity or even mortality. Midazolam and thiopentone are commonly used anaesthetics in this condition. Since early reports of experience of using ketamine in SRSE nearly two decades ago, its role in clinical practice is still uncertain. The study aims to evaluate the utility of ketamine in SRSE in children in a tertiary centre in Hong Kong

Methods: Records were retrieved from Clinical Management System (CMS) for patients who were admitted from 1 Jan 2011 to 31 Dec 2017 for super-refractory status epilepticus, with particular focus on the anaesthetics used. Demographic data, aetiological investigations, treatment, complications and outcome were recorded.

Results: Fifteen patients were admitted for SRSE during the period. Patients with known epilepsy/ epileptic encephalopathy with SRSE were excluded. There were four females. Age of the patients range from 28 months to 16 years (median ~8years old). Duration of ICU stay ranged from 4 days to 6.5 months (median 21 days). Among these patients, three of them had used ketamine as anaesthetic

agent at a rage of 2-3 mg/kg/hour. They had been put on it from day 7-15 of anaesthesia for 1 day to 29 days. All patients tolerated it well without need to push up inotropes or blood abnormalities.

Conclusions: Ketamine is generally well tolerated and efficacious in children. It is used > 7 days of anaesthesia. The potential of early use in SRSE is an attractive alternative. Although it has been included in algorithms for SRSE, its acceptance and understanding among intensive care physicians is still relatively low. Its role and utility remain to be defined.

P73

Super refractory status epilepticus in a patient with Lafora disease treated with vagus nerve stimulation

Francesca Bisulli¹, Barbara Mostacci², Lorenzo Muccioli¹, Irene Minardi², Marco Bandini², Laura Licchetta¹, Chiara Leta¹, Roberto Michelucci², Marco Zanella¹, Paolo Tinuper¹

¹IRCCS Istituto delle Scienze Neurologiche, Dipartimento di Scienze Biomediche e Neuromotorie, Università di Bologna, Bologna, Italy, ²IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy

Background: Vagus nerve stimulation (VNS), an effective therapy for drug-resistant epilepsy, has been used with inconsistent results in super refractory status epilepticus (SRSE). There is no available protocol and data on long term prognosis on this approach are lacking. We present a case in which VNS was used in a patient with SRSE affected by Lafora disease, a rare, lethal, progressive myoclonus epilepsy.

Methods: The patient underwent a complete clinical and diagnostic assessment, including genetic testing and histopathological examination. Multiple associations of antiepileptic and anesthetic drugs were attempted to treat the SRSE under continuous video-EEG monitoring. VNS was switched on in the intensive care unit (ICU) immediately after implantation. The following parameters were obtained within the fifth post-operative day: intensity 1.75 mA, pulse width 500 mcs, frequency 30 Hz, duty cycle 30" on-1.8 ' off, magnet 2 mA.

Results: A girl affected by histopathologically and genetically confirmed Lafora disease, with epilepsy onset at 13 years, presented a SRSE at 16 years, eight months after her seizures became drug-resistant. While in ICU, we tried eight different second-line and four third-line therapies in multiple associations, as well as ketogenic diet, immunotherapy, and allopregnenolone treatment.

Anesthetic weanings were attempted several times and were followed by recurrence of an electric status or clusters of tonic-clonic seizures. Following VNS implantation, after two months from SRSE onset, we were able to wean third line agents. Since then, the patient presented a single cluster of tonic-clonic seizures. However, consciousness remained compromised and she kept on having subcontinuous myoclonic jerks until her death, occurred nine months later for tracheostomy-related late bleeding.

Conclusion: We report a case of SRSE complicating a Lafora disease successfully treated with VNS and provide details of the adopted titration scheme. Even though the outcome was poor, probably due to the severity of the underlying disease and the long time spent in ICU on third-line agents, these findings may be useful for clinicians, as no VNS titration protocol in SRSE is available and being this the first case report in which VNS was adopted to treat this condition in Lafora disease.

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Super-refractory status epilepticus with persisting seizures and treatment-related complications: Case report

Johan Bjellvi, Anna Edelvik, David Krysl, Josefin Nilsson, Johan Zelano, Helena Odenstedt Herges

Sahlgrenska University Hospital, Gothenburg, Sweden

Background: In refractory status epilepticus (SE), treatment protocols advocate induction of therapeutic coma titrated towards electrographic seizure suppression, burst suppression or, in some cases, complete background suppression. However, the use of anaesthetics has been associated with worse outcome in refractory SE, and high doses of these agents are often required to achieve the desired EEG endpoint.

Methods: Based on medical records, we describe a case of super-refractory SE with fatal outcome, where seizures were resistant to any available therapy, and where anaesthetic treatment was hampered by serious adverse effects. The patient's parents gave informed consent for the report.

Results: A 23-year-old female with unremarkable medical history was admitted with convulsive SE preceded by four days with headache, fever and dizziness. CSF showed moderate leucocytosis. MRI showed symmetrical limbic signal enhancements. Autoimmune encephalitis was suspected, but CSF was negative for autoimmune and paraneoplastic antibodies as well as for viral and

bacterial infections. Consecutive immune therapies tried were methylprednisolone, IVIG, plasmapheresis, and rituximab. Antiepileptic therapies given were fosphenytoin, valproate, levetiracetam, lacosamide, and topiramate. Complementary therapies were magnesium and ketogenic diet. Therapeutic coma was induced with propofol and midazolam, but propofol was paused due to increasing lactate. Thiopental was added but withdrawn because of cardiotoxicity. Treatment was continued with propofol, midazolam, and ketamine, and circular stability was regained. Due to persisting seizures, thiopental was reintroduced at a lower rate. The patient slowly developed multiple organ failure and increasing cardiovascular instability. Despite efforts to stabilize the patient, she died from massive circulatory collapse and general brain oedema on day 19 with SE. During the whole period, EEG showed continuous or repeated seizures, including electrographic seizures emerging from a burst suppression or isoelectric background, with only short periods of seizure freedom with isoelectric background.

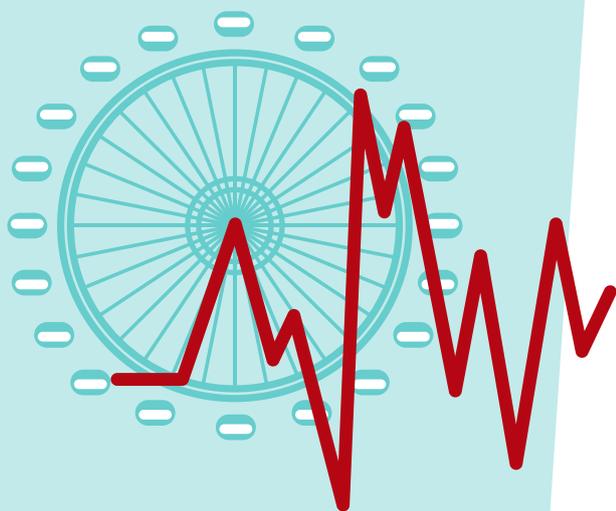
Conclusions: In super-refractory SE, electrographic seizure suppression can be difficult to achieve. Treatment targets indicated in existing guidelines have to be balanced against the risk for treatment-related adverse effects. Close monitoring of the EEG background is needed. Clinical decisions are informed by detection of electrographic seizures, but their interpretation can be demanding in the context of suppressed background activity.



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**THE
8TH LONDON-INNSBRUCK
COLLOQUIUM
ON STATUS EPILEPTICUS
AND ACUTE SEIZURES**

**APRIL 2021
VIENNA, AUSTRIA**



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COLLOQUIUM DINNER AT THE ATHENAEUM CLUB

Sunday, April 7th, 2019

19.30 – 24.00

The conference dinners at the Status Epilepticus Colloquia are famously entertaining. This time, the dinner is being held at the Athenaeum Club – one of the grandest of the London Clubs and its most intellectual. Named after Athena, the goddess of wisdom, club members have included 52 Nobel Prize winners and, at a more humble level, many neurologists and neurosurgeons including the founding fathers of epilepsy such as David Ferrier, William Gowers and Victor Horsley. Dinner will be a sumptuous affair as the club is famous for the quality of its food and wine. The 19th century dining room (bizarrely called the coffee room) and the drawing rooms are amongst the most splendid in London. Michael Faraday’s iron-tyred wheelchair is available (but only to view) for those feeling unable to walk back to the hotels.

It should be an enjoyable and entertaining diversion; and all delegates are invited to join the faculty to celebrate the spirit of our Colloquium – starting, of course, with a glass of the club champagne.

Dress code: smart casual
Web: athenaeumclub.co.uk
Address: 107 Pall Mall, London
SW1Y 5ER (closest
underground station:
Piccadilly Circus)



YES – YOUNG EPILEPSY SECTION EVENT

Monday, April 8th, 2019

19.00 – 21.00 at Hurricane Room

Dear Junior/Student attendee of the Status Colloquium,
Interested in networking with other early career clinicians and researchers working in epilepsy in an informal and relaxed environment? Then please join us for an opportunity to unwind, meet each other and play some pool after spending the day at the Status Colloquium!
The event is organised by YES (Young Epilepsy Section) of the ILAE and will be held at Hurricane Room, 368 Grays Inn Rd, London WC1X 8BB.
Pool tables, small snacks and a drink voucher will be provided.



CONFERENCE VENUE

The Francis Crick Institute
1 Midland Road
London NW1 1ST

REGISTRATION DESK

The registration will be located on the ground floor of the Francis Crick Institute. Please note that access to the Crick is strictly controlled and will be possible with your name badge only. On Sunday, delegates are admitted from 08.00 am to register. Opening hours are as follows:

Sunday, 7 April: 08.00 – 17.00
Monday, 8 April: 07.45 – 17.30
Tuesday, 9 April: 07.45 – 17.00

CONGRESS ORGANISERS

PCO Tyrol Congress
Congress und Messe Innsbruck GmbH
Rennweg 3
6020 Innsbruck, Austria
E: status@cmi.at
I: www.cmi.at



CERTIFICATE OF ATTENDANCE

All registered delegates receive an official certificate of attendance after the conference by email together with a survey about the colloquium.

CPD CREDITS

The 7th London-Innsbruck Colloquium has been accredited with 18 CPD points (category 1 points) by the Federation of Royal College of Physicians of the United Kingdom

TRADE EXHIBITION

A trade exhibition of pharmaceutical companies and manufacturers of medical equipment is held next to the Wellcome Auditorium.

EXHIBITION ORGANISERS

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



COFFEE BREAKS AND REFRESHMENTS

Coffee and tea as well as light lunches will be served during the official breaks.

NAME BADGES

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

LIABILITY AND INSURANCE

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

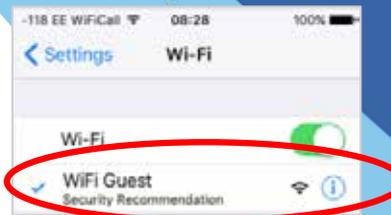
WI-FI ACCESS

There is free Wi-Fi access at the Crick Institute. See opposite page for instructions.

Connecting to guest Wi-Fi

1

Connect to the **Wi-Fi Guest** network on your device



2

Open your browser and go to a non-secure website – <http://www.bbc.co.uk>, for example



3

Tap **Get online at The Francis Crick Institute**



4

If you have not used The Cloud before, tap **Create Account** and enter your details

If you have used The Cloud elsewhere – in railway stations, restaurants, pubs and so on – you can enter the email and password that you have previously set up yourself and tap **Continue**



5

You are now connected to the guest Wi-Fi



Premature mortality in epileptic encephalopathies: Towards a better understanding



Monday 8th April 2019, 13.00-14.00

Chairman: Professor Matthew Walker (London, UK)

-
- 13.00 - 13.05 ■ **Welcome and Introduction**
Matthew Walker
-
- 13.05 - 13.20 ■ **The Value of Preclinical Models?**
Benoit Martin (Rennes, France)
-
- 13.20 - 13.35 ■ **Neuropathology: Insights and Challenges**
Maria Thom (London, UK)
-
- 13.35 - 13.50 ■ **Clinical and Family/Patient perspectives**
Richard Chin (Edinburgh, UK)
-
- 13.50 - 14.00 ■ **Where Might Such Understanding Lead Us?**
Matthew Walker

ZOGENIX