

Encephalopathy related to Status Epilepticus during slow Sleep: linking epilepsy, sleep disruption and cognitive impairment

Guest Editors:
Guido Rubboli
Carlo Alberto Tassinari

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Contents

List of authors	VII
Preface	XI
Linking epilepsy, sleep disruption and cognitive impairment in Encephalopathy related to Status Epilepticus during slow Sleep (ESES) <i>Guido Rubboli, Carlo Alberto Tassinari</i>	1
Encephalopathy related to Status Epilepticus during slow Sleep: an historical introduction <i>Guido Rubboli, Carlo Alberto Tassinari</i>	3
Encephalopathy related to Status Epilepticus during slow Sleep: from concepts to terminology <i>Edouard Hirsch, Roberto Caraballo, Bernardo Dalla Bernardina, Tobias Loddenkemper, Sameer M. Zuberi</i>	7
A commentary on Encephalopathy related to Status Epilepticus during slow Sleep: from concepts to terminology <i>Carlo Alberto Tassinari, Guido Rubboli</i>	17
Encephalopathy with continuous spike-waves during slow-wave sleep: evolution and prognosis <i>Roberto Caraballo, Elena Pavlidis, Marina Nikanorova, Tobias Loddenkemper</i>	19
EEG features in Encephalopathy related to Status Epilepticus during slow Sleep <i>Elena Gardella, Gaetano Cantalupo, Pål G. Larsson, Elena Fontana, Bernardo dalla Bernardina, Guido Rubboli, Francesca Darra</i>	25

Quantitative EEG analysis in Encephalopathy related to Status Epilepticus during slow Sleep <i>Gaetano Cantalupo, Elena Pavlidis, Sandor Beniczky, Pietro Avanzini, Elena Gardella, Pål G. Larsson</i>	37
Update on the genetics of the epilepsy-aphasia spectrum and role of GRIN2A mutations <i>Gaetan Lesca, Rikke S. Møller, Gabrielle Rudolf, Edouard Hirsch, Helle Hjalgrim, Pierre Szepietowski</i>	49
Pathophysiology of encephalopathy related to continuous spike and waves during sleep: the contribution of neuroimaging <i>Michael Siniatchkin, Patrick Van Bogaert</i>	55
Interictal epileptiform discharges in sleep and the role of the thalamus in Encephalopathy related to Status Epilepticus during slow Sleep <i>Steve A. Gibbs, Lino Nobili, Péter Halász</i>	61
Encephalopathy related to Status Epilepticus during slow Sleep: a link with sleep homeostasis? <i>Guido Rubboli, Reto Huber, Giulio Tononi, Carlo Alberto Tassinari</i>	69
Cognitive impairment and behavioral disorders in Encephalopathy related to Status Epilepticus during slow Sleep: diagnostic assessment and outcome <i>Alexis Arzimanoglou, Helen J. Cross</i>	77
Progressive intellectual impairment in children with Encephalopathy related to Status Epilepticus during slow Sleep <i>Liam Dorris, Mary O'Regan, Margaret Wilson, Sameer M. Zuberi</i>	83
Current treatment options for Encephalopathy related to Status Epilepticus during slow Sleep <i>Floor E. Jansen, Marina Nikanorova, Maria Peltola</i>	93
Encephalopathy related to Status Epilepticus during slow Sleep: current concepts and future directions <i>Carlo Alberto Tassinari, Guido Rubboli</i>	99
References	105

List of authors

Alexis Arzimanoglou, Department of Paediatric Clinical Epileptology, Sleep Disorders and Functional Neurology, University Hospitals of Lyon (HCL), Member of the European Reference Network EpiCARE, Lyon, France
Epilepsy Unit Hospital San Juan de Dios, Member of the ERN EpiCARE and Universitat de Barcelona, Barcelona, Spain

Pietro Avanzini, Neuroscience Department, University of Parma, Parma, Italy

Sandor Beniczky, Department of Clinical Neurophysiology, Danish Epilepsy Centre, Dianalund University of Aarhus, Aarhus, Denmark

Gaetano Cantalupo, Department of Child Neuropsychiatry, Department of Life and Reproduction Sciences, University of Verona, Italy

Roberto Caraballo, Department of Neurology, Pediatric Hospital Prof. Dr. Juan P Garrahan, Buenos Aires, Argentina

Helen J. Cross, UCL-Great Ormond Street Institute of Child Health, Great Ormond Street Hospital for Children NHS Trust, Member of the European Reference Network EpiCARE, London, UK

Bernardo dalla Bernardina, Department of Child Neuropsychiatry, Department of Life and Reproduction Sciences, University of Verona, Italy

Francesca Darra, Department of Child Neuropsychiatry, Department of Life and Reproduction Sciences, University of Verona, Italy

Liam Dorris, Paediatric Neurosciences Research Group, Royal Hospital for Children Institute of Health and Wellbeing, University of Glasgow, Member of the European Reference Network EpiCARE, Glasgow, UK

Elena Fontana, Department of Child Neuropsychiatry, Department of Life and Reproduction Sciences, University of Verona, Italy

Elena Gardella, Department of Clinical Neurophysiology, Danish Epilepsy Centre, Dianalund University of Southern Denmark, Odense, Denmark

Steve A. Gibbs, Centre for Epilepsy Surgery “C. Munari”, Centre of Sleep Medicine, Department of Neuroscience, Niguarda Hospital, Milan, Italy
Centre for Advanced Studies in Sleep Medicine, Dept. of Neurosciences, Hôpital du Sacré-Coeur de Montreal, Université de Montréal, Montréal, Canada

Peter Halasz, National Institute of Clinical Neuroscience, Budapest, Hungary

Edouard Hirsch, Centre de référence et d'exploration des épilepsies, Pôle Tête Cou / CETD, Neurologie CHU de Strasbourg, Hôpital de Hautepierre, Strasbourg, France
Fédération de Médecine Translationnelle (FMTS), Strasbourg, France
INSERM UMR_SU1119, Strasbourg, France

Helle Hjalgrim, Danish Epilepsy Centre, Dianalund, Denmark
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Reto Huber, Child Development Centre, University Children's Hospital Zurich, Switzerland

Floor E. Jansen, Department of Child Neurology, Brain Center, University medical Center Utrecht, Member of the European Reference Network EpiCARE, The Netherlands
Children's Department, Danish Epilepsy Centre, Dianalund, Denmark

Pal G. Larsson, Department of Neurosurgery, Oslo University Hospital, Oslo, Norway

Gaetan Lesca, Department of Genetics, University Hospitals of Lyon, Member of the European Reference Network EpiCARE Lyon, France
Claude Bernard Lyon I University, Lyon, France
Centre de Recherche en Neurosciences de Lyon, CNRS UMR5292, INSERM U1028, Lyon, France

Tobias Loddenkemper, Division of Epilepsy and Clinical Neurophysiology, Department of Neurology, Boston Children's Hospital, Boston, MA, USA

Rikke S. Møller, Danish Epilepsy Centre, Dianalund, Denmark

Marina Nikanorova, Danish Epilepsy Centre, Dianalund, Denmark

Lino Nobili, Centre for Epilepsy Surgery "C. Munari", Centre of Sleep Medicine, Department of Neuroscience, Niguarda Hospital, Milan, Italy
Child Neuropsychiatry, IRCCS, G. Gaslini Institute, Dept. of Neuroscience (DINO GMI), University of Genoa, Italy

Mary O'Regan, Paediatric Neurosciences Research Group, Royal Hospital for Children, Glasgow, UK

Elena Pavlidis, Child Neuropsychiatry Unit, Neuroscience Department, University of Parma, Italy
Danish Epilepsy Centre, Dianalund, Denmark

Maria Peltola, HUS Medical Imaging Center, Clinical Neurophysiology, University of Helsinki, Helsinki University Hospital and University of Helsinki, Finland

Guido Rubboli, Danish Epilepsy Center, Filadelfia, University of Copenhagen, Dianalund, Denmark

Gabrielle Rudolf, Fédération de Médecine Translationnelle (FMTS), Strasbourg, France
IGBMC, CNRS UMR7104, INSERM U964, Strasbourg University, France
INSERM UMR_SU1119, Strasbourg, France

Michael Siniatchkin, Institute of Medical Psychology and Medical Sociology, Christian-Albrechts-University of Kiel, Germany

Pierre Szepetowski, Aix-Marseille University, INSERM UMR1249, INMED, Marseille, France

Carlo Alberto Tassinari, University of Bologna, Bologna, Italy

Giulio Tononi, Department of Psychiatry, University of Wisconsin, Wisconsin, USA

Patrick Van Bogaert, Department of Pediatric Neurology, CHU d'Angers, and Laboratoire Angevin de Recherche en Ingénierie des Systèmes (LARIS), Université d'Angers, France

Margaret Wilson, Paediatric Neurosciences Research Group, Royal Hospital for Children, Glasgow, UK

Sameer M. Zuberi, Paediatric Neurosciences Research Group, Royal Hospital for Children & University of Glasgow, Member of the European Reference Network EpiCARE, Glasgow, UK

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Preface

The interactions between epilepsy, sleep and cognition are complex and reciprocal. Experimental and clinical findings have clearly shown that sleep is beneficial for cognition by actively participating in learning, language acquisition and memory consolidation. These evidences imply that chronic sleep disturbances, particularly in the critical period of brain maturation, may have adverse effects on learning and normal neuropsychological development. In this respect, Encephalopathy related to Status Epilepticus during slow Sleep (ESES), an age-related epileptic syndrome characterized by deterioration of cognitive functions and behavior, epileptic seizures, and extreme activation of EEG epileptiform discharges during non-REM sleep, can represent a privileged model to investigate the deleterious effect of prolonged sleep-related epileptic activity in the developmental age on cognition and behavior. However, in spite of the fact that ESES has been first described almost 50 years ago and that a considerable amount of clinical observations and neurophysiological, neuroimaging, and genetic findings have been accumulated, several issues related to ESES, including the very definition of this condition and its nosology, are still debated and the pathophysiological mechanisms underlying the cognitive and behavioral derangement associated with the appearance of exaggerated sleep-related epileptic activity are poorly understood.

The series of chapters included in this book provides an updated overview on the current knowledge on ESES. Topics such as the clinical and EEG features necessary for the diagnosis, the neurophysiologic and neuropsychological diagnostic assessments, the various therapeutic approaches and the most recent neuroimaging and genetic findings are reviewed with a focus on the most novel aspects. In addition, the fascinating perspectives opened by recent evidences suggesting that the pathophysiological mechanisms underlying the cognitive/behavioral disturbances occurring in ESES might be related to impaired sleep homeostasis caused by prolonged sleep-related epileptic activity are discussed. These latter findings raise the issue that apparently subclinical epileptic activity during sleep might be predicted to have clinical relevance whether appropriately tested (with careful neuropsychological, neuroimaging and neurophysiological testing including also the analysis of EEG parameters assessing sleep homeostasis), not only in ESES but also in larger populations of children with other childhood epilepsies with striking enhancement of epileptic discharges during sleep.

Indeed, we present this book with the intent to identify concepts for which there is a shared view and consolidated knowledge as well as areas where there are still disagreements or controversies and lack of information demanding further studies and research.

This work would have not been possible without the invaluable contribution of the clinicians, neurophysiologists, sleep physiologists and geneticists who have studied ESES and who have taken the burden to contribute their chapters. To them we wish to express our deep appreciation.

Finally, we are very grateful to Prof. Alexis Arzimanoglou at *Epileptic Disorders* for his continuous support and guidance through the manuscript collection and the editing process and to the staff of John Libbey Eurotext for their trademark competence and dedication.

Guido Rubboli, Carlo Alberto Tassinari

Linking epilepsy, sleep disruption and cognitive impairment in Encephalopathy related to Status Epilepticus during slow Sleep (ESES)

Guido Rubboli, Carlo Alberto Tassinari

“Encephalopathy related to Status Epilepticus during slow Sleep (ESES)” was described more than forty-five years ago in a small group of children with learning disabilities who displayed a peculiar EEG pattern consisting of apparently “sub-clinical” spike-and-wave discharges, that occurred almost continuously during sleep for a variable length of time (months to years). Later on, the condition of a protracted “status epilepticus during sleep” (SES) in the developmental age was proposed to be the factor leading to the appearance of severe cognitive and psychic disturbances. Indeed, the extreme activation of epileptic activities during NREM sleep still stands as the electroencephalographic hallmark of a condition that, if prolonged, causes the appearance of a clinical picture that has been acknowledged to be an encephalopathy related to SES. From a broader perspective, SES may be responsible not only for cognitive dysfunctions, such as for instance acquired aphasia, *i.e.* *Landau-Kleffner syndrome*, but also (and often concomitantly) for other dysfunctions, such as severe behavioral disorders and motor impairment (*i.e.* apraxia and negative myoclonus). Etiology of ESES can be heterogeneous as well, in fact it has been reported in children with organic brain lesions as well as in children with an epilepsy of benign evolution - whether idiopathic or cryptogenic.

After hundreds of observations and comprehensive reviews on the subject (including a monography on the Venice Symposium edited by [Beaumanoir et al. in 1995](#)), it became clear that SES, cognitive impairment and behavioural disturbances evolve in parallel, and in fact when these latter disorders recover, SES tends to disappear (or it is already over). However, in spite of the wealth of data accumulated over decades, the clinical spectrum of ESES and its boundaries, the diagnostic criteria, the pathophysiology and the therapeutic management are still a matter of debate.