INTERNATIONAL LEAGUE AGAINST EPILEPSY
Established 1909

Epileptic Disorders
THE EDUCATIONAL JOURNAL OF THE INTERNATIONAL LEAGUE AGAINST EPILEPSY

Vol. 21, June 2019 - Supplement 1

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

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Epileptic Disorders

The Educational Journal of the International League Against Epilepsy

http://www.epilepticdisorders.com

ISBN: 978-2-7420-1616-7
ISSN: 1294-9361

Published by
Éditions John Libbey Eurotext
127, avenue de la République, 92120 Montrouge, France
Tel.: +33 (0)1 46 73 06 60
www.jle.com

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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.