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New epilepsy-taxonomy based on the system epilepsy concept – A mini-review and proposal

Péter Halász[1] and Anna Szűcs[2]

[1]Pécs University of Sciences, Department of Neurology and Epileptology
[2]Semmelweis University, Institute of Behavioural Sciences, Budapest

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ABSTRACT

In this review we propose a new epilepsy-taxonomy, based on recent sleep- and epilepsy research. It has been evidenced that sleep is a "cradle" of human cognitive development, and epileptogenesis – as an inbuilt risk - is underlined by the pathologic increase of the homeostatic NREM sleep regulation and the derailment of synaptic plasticity. Therefore, NREM sleep has an essential role in epileptogenesis and across the course of epilepsies. This approach goes hand in hand with the emerging system-concept abolishing the "Procrustean bed" of the now untenable focal-generalized epilepsy classification.

Based on the system-approach, we briefly reinterpret the most frequent epilepsies each presenting with system-specific features both ictally and interictally while sharing the common mechanism of disfigured epileptic "learning".

Introduction

Sleep research has provided important aspects on the reason why sleep persists across the phylogeny and takes one third of human life.

First it has become evident that the amount of sleep is regulated by the duration of the preceding waking-time.[1] Then it has turned out that not the duration, rather the degree of synaptic use is decisive.[2,3] An emblematic experiment showed that the strong vibration of the arm in waking, resulted in an increase of delta-activity over the cortical representation-field of that arm in the next sleep.[4]

We have learned that sleep is under use-dependent homeostatic regulation best represented by EEG slow wave activity (SWA), a substrate and measure of NREM sleep homeostasis. During the day, homeostatic pressure increases paralleling sleep-propensity and EEG SWA. When we fall asleep, SWA continues increasing during the first sleep cycles; then it decreases exponentially in the subsequent ones. Slow wave activity seems to be necessary for recovering synaptic capacity for the next day, however, the mechanism of this process remains unclear.[2,3,5] It has been evidenced, too, that use-dependent slow wave homeostasis boosts homeostatic plasticity. Therefore, sleep homeostasis goes hand in hand with the increase of plasticity, providing multilevel support to learning and to the adaptability of our brain. (Fig 1)

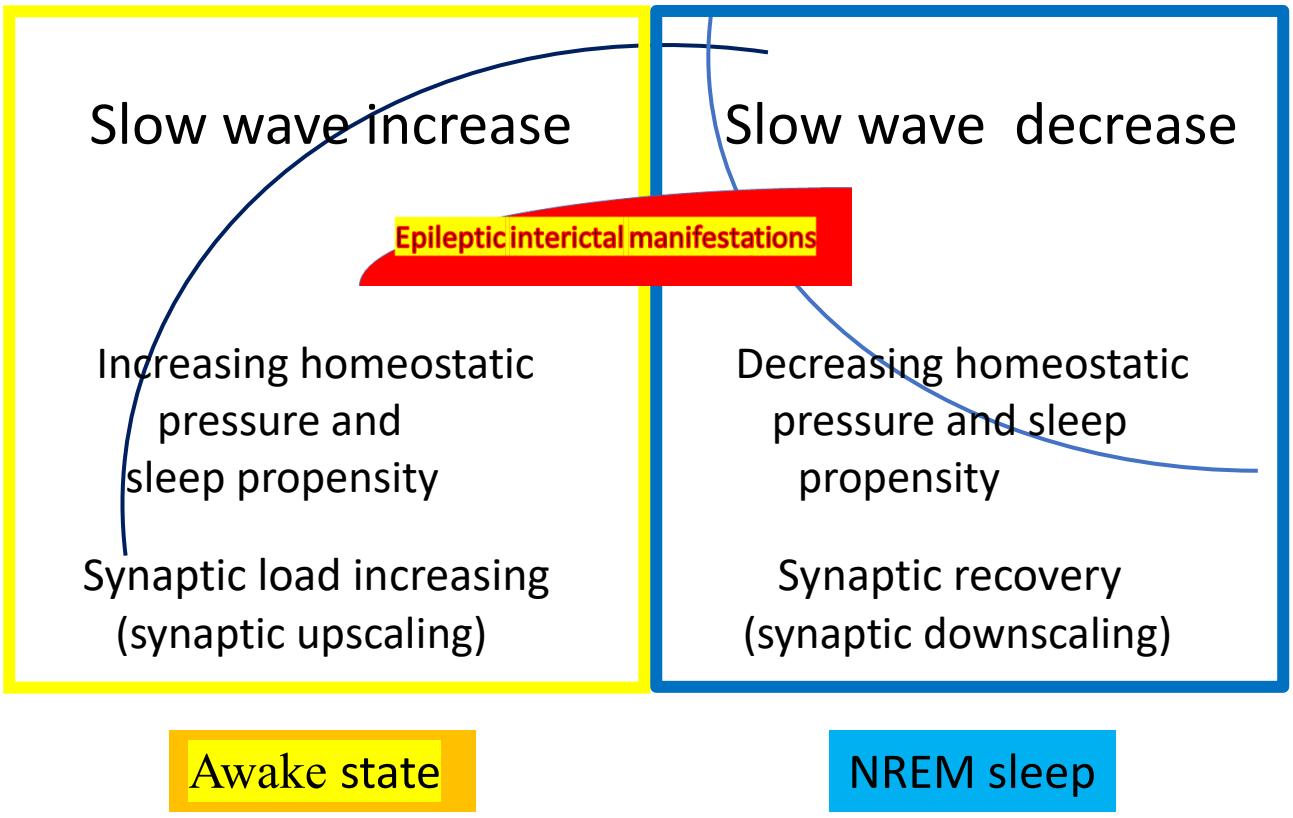

Fig. 1: Slep propensity, homeostatic pressure, sleep slow waves, and synaptic economy, during awake state and NREM sleep. In awake state the homeostatic pressure, the amount of slow waves, and the synaptic load increase exponantially, durinthe first cycles of sleep; the homeostatic pressure, the slow wave power, and the sleep propensity is highest. later decrease together with the synaptic revovery exponentially. The red/yellow insert indicate the degree of interictal epileptic manifestationsm being the highest amount during the end of day and the first sleep cycles. Yellow square= wake, blue = square sleep state.

Here we arrive to epilepsy; suspected for long to be resulted by a derailment (exaggeration) of plasticity; a chronic increase of excitability in the archi-, and neocortex; that may lead to epileptic seizures. Buzsáki[6] remembered the work of Goddard[7] first supposing that the plastic processes of memory engram-formation and epileptogenesis are similar. The repetitive stimulation of a neuron may generate long term potentiation (LTP) in a synaptically connected one, resulting in engram-formation. Similarly, in epileptic kindling, the enduring stimulation of epilepsy-prone brain structures leads to after-discharges and epilepsy. If epilepsy starts in early life at the time of intensive development, the epileptic over-excitation may alter the function of the affected brain systems, based on the Hebbian „firing together, wiring together" principle, and take over their regulation. Beenhakker and Huguenard[8] called this epileptic learning the „hijacking" of certain brain systems. The assumption that epilepsy would be a derailment of inherent plasticity, seems plausible. This approach explains the high prevalence of epilepsy and make it the by-product of the ability to learn.

Therefore Tononi's witty idea: epilepsy is the price of plasticity seems valid. In other words, sleep homeostatic plasticity carries the risk for epileptic upregulation[5].

In recent years, there is increasing interest in the relationship of sleep and epilepsy. Most papers deal with sleep disorders [10-13], affecting people with epilepsy, and call attention to the cognitive harm of those sleep disturbances. This is an important aspect, but just a few works focus on its reverse: the augmenting effect of NREM sleep on epilepsy[9].

The development of epilepsy is a long process that remains hidden before the first epileptic seizures appear. The first hit triggering this process may be a genetic change or any brain lesion; going unnoticed until epilepsy highlight them. The histological analyses of resected epileptic brain-specimens have revealed those years-lasting transformations evolving between the first hit and the appearance of epileptic symptoms[14].

The relationship of interictal EEG activity and clinical seizures is not fully understood. The localisation, timing and types of spiking and seizures are variable. There are no long-term follow-up studies of spiking in self-limiting epilepsies and the appearance of seizures after symptomless spiking periods is not enough studied. At the same time, the leading roles of interictal spiking surpassing those of seizures in certain epilepsies, highlight their epileptogenic significance.

Longitudinal tracking of patients after successful epilepsy-surgery, reveal a running-down of spikes supporting their significance, and show high-frequency oscillations as important severity-markers of epilepsy; giving support to the importance of interictal activity as well.

System-epilepsies as the building stones of a new epilepsy taxonomy

The emerging system-epilepsy concept has not been built into the prevailing concept of epileptogenesis[15-18].This approach requires functional anatomic knowledge of the affected systems. Reflex-triggers are required to be congruent with the function of the system (Fig 2) and also seizure-symptoms need to represent it in a positive or negative way, e.g. memory disturbances in mesiotemporal seizures, focal motor symptoms in seizures of the motor system. The localisation of EEG symptoms and imaging alterations need to cover the system's anatomy (e.g. hippocampal sclerosis in the epilepsy of the memory system) and long-term functional deficits related to system-features need to be recognised (e.g. neuropsychological deficits in perisylvian epilepsies (see later).

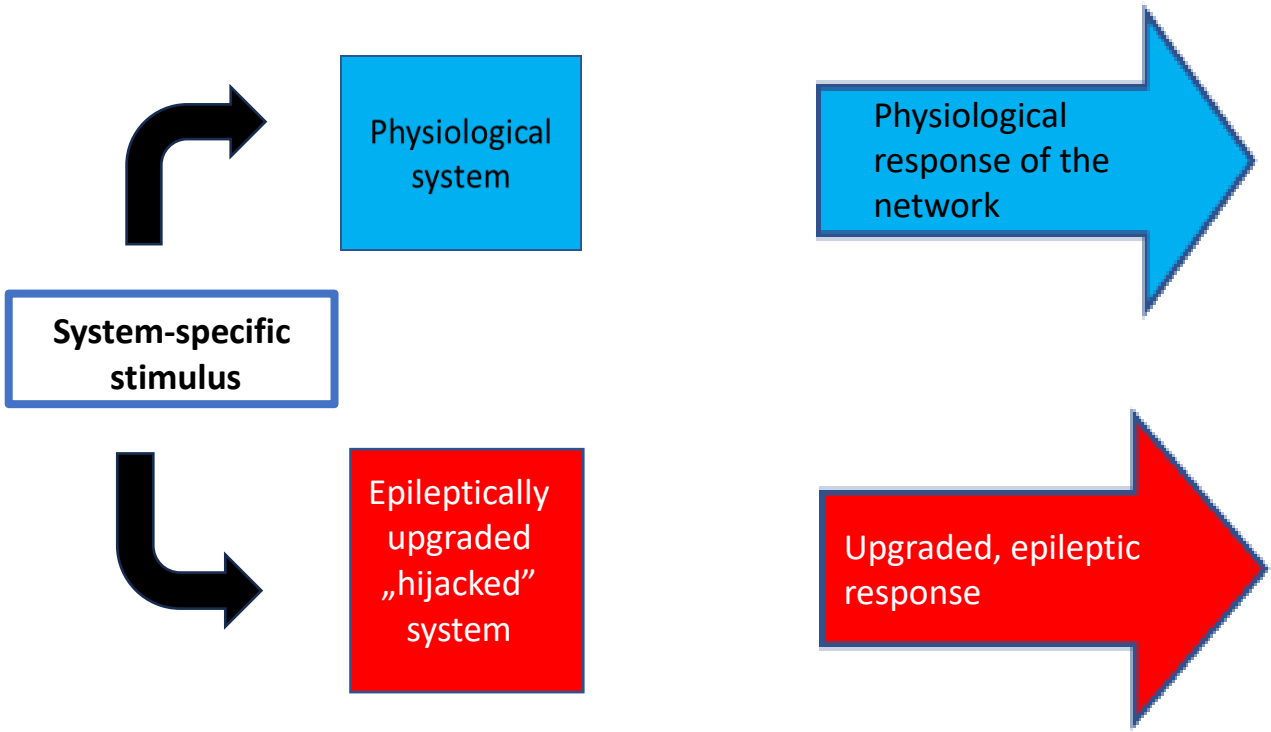

Fig. 2: Upper panel: Schematic view of the physiological and epileptical activation by system specific stimuli and by putting into motion of the systems by previously upgraded epileptic systems. System specific afferent stimuli evoke system specific system responses, while epiletically facilitated (upgraded) systems respond with system specific seizures.

Lower panel:Certain sleep related systems (for example falling in sleep or arousal from sleep) triggers system specific seizures.

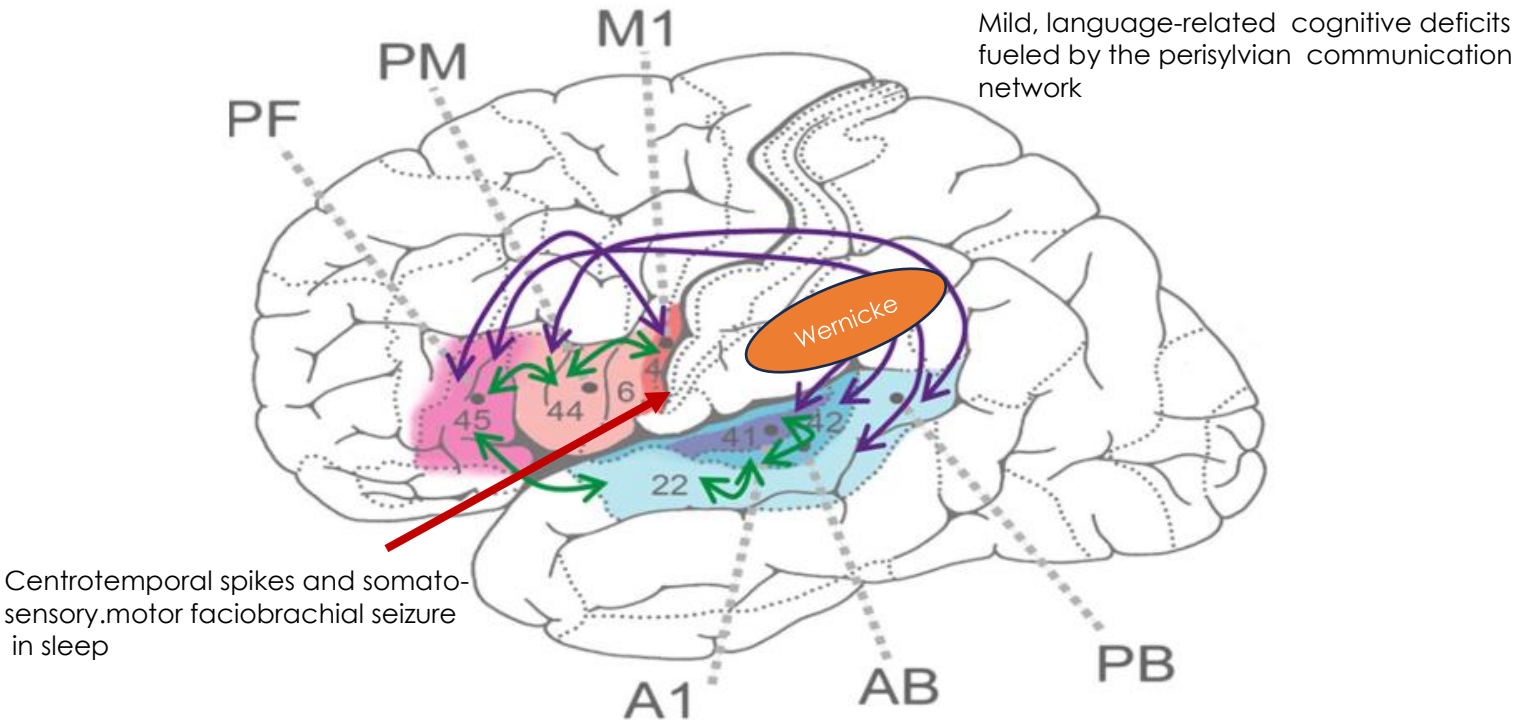

Fig. 3: Schematic view of the perisylvian human communication. System specific network with representation of speach, reading writing, hearing linguistic and musical functions. A1, AB, PB = acoustic, PF, PM, MI =prefrontal. premotor and motor fields, The red arrow points to the onset zones of centrotemporal spikes and focal facio-brachial seizures. The upper right texts charactrizes the widespread mild cognitive impairment detected by neuropsychological studies Schematic view of physiologic (blue) and epileptically upgraded (red) brain nerworks response activated by the same system specific afferent stimuli. (After Schomers et al modified[26])

Epilepsies re-classified based on the system-concept

MEDIAL TEMPORAL LOBE EPILEPSY (THE MOST FREQUENT EPILEPSY OF ADULTHOOD): AN EPILEPSY OF THE DECLARATIVE MEMORY SYSTEM

Typical structural abnormality is the hippocampal sclerosis or any anterior temporal lesion affecting the hippocampus and/or amygdala. An epileptic histological and electro-morphological transformation produces the anterior temporal EEG spikes and the focal onset seizures with gastrointestinal, emotional and memory symptoms. Long term declarative memory deficit (with diagnostically important side-differences) may evolve. This memory deficit is caused by the chronic deficit of memory consolidation; due to hippocampal sharp wave–ripples' (essential in memory consolidation) transformation to epileptic spikes and pathological high frequency (> 200 Hz) ripples[19,20]. Consequently, the damaged but discharging hippocampus sends nonsense messages to the frontal lobe, disturbing the NREM sleep-related hippocampo-frontal correspondence and distorting the consolidation of memory.

ABSENCE EPILEPSY: AN EPILEPSY OF THE THALAMOCORTICAL NETWORK AND NREM SLEEP-PROMOTION.

The main symptoms are brief interruptions of consciousness (absences) in childhood, occurring in the transition-periods between wakefulness and NREM sleep. Full wakefulness and REM sleep inhibit them. The burst-firing working mode of the thalamic reticular nucleus involving cortical pyramidal neurons and the thalamic relay cells, produces slow waves and sleep spindles, the typical EEG pattern of NREM sleep. A genetic mutation affecting GABAergic intra-reticular inhibition may reverse this system to produce 3-4 Hz bilateral spike-waves[21], the EEG pattern of absences, instead of spindles. Recent studies have revealed a more complex regulation with cortical driver zones and the basal ganglia's participation[22].

JUVENILE MYOCLONIC EPILEPSY (JME): AN EPILEPSY OF THE THALAMOCORTICAL NETWORK

It is in spectral link with absence epilepsy, involving broader cortical fields.

It appears between the teenage years and young adulthood and may last life-long.

JME and absence epilepsy share absence seizures, but in JME, the main seizure type is myoclonus - jerking of the limbs - and generalized tonic-clonic (GTC) seizures. JME is remarkably sensitive for sleep-deprivation (i.e. the elevation of homeostatic pressure). Due to globally increased cortical excitability, variable (visual, sensory-motors etc.) stimuli can act as reflex seizure-triggers; e.g. in the form of photo-myoclonic jerks, among others.

SLEEP-RELATED HYPERMOTOR EPILEPSY (SHE): AN EPILEPSY OF AROUSAL FROM NREM SLEEP, underlined by genetic mutations modifying the function of the ascending brainstem reticular arousal-system. Mutations of the CHRNA4, CHRNB2 CHRNA2 genes encoding the neuronal acetylcholine receptor (α4, β2, and α2 subunits, respectively) were found in 10–20% of SHE patients with a positive family history but just in 5% of sporadic cases[23].

These mutations affect the pore-forming M2 transmembrane segments, likely causing increased sensitivity to acetylcholine. In addition, mutations in the corticotropin-releasing hormone (CRH) gene of locus 15q[24] containing genes, have been identified in patients with SHE Patients experience hyperarousal with epileptic level over-shoots of excitation culminating in NREM sleep.

This epilepsy seems to be the Yin-Yang counterpart of absence epilepsy, nestling in the sleep-promoting system. Newly, some doubt has emerged around the epileptic nature of hypermotor seizures. We[24] have raised the possibility that not all symptoms of hypermotor seizures are epileptic; some may represent a Cannon-Selye stress response ignited by the salience network, which is activated by ictal excitation of the fronto-medial region.

SENSORY-MOTOR EPILEPSY: AN EPILEPSY OF THE SENSORY-MOTOR SYSTEM

This epilepsy may evolve due to any developmental or lesional change of the primary sensory-motor cortex. The motor seizures are ignited by movement initiation or sensory impulses. Neuroimaging may reveal the underlying focal changes, and the ictal/interictal EEG coincides with those sites.

VISUAL EPILEPSY: AN EPILEPSY OF THE VISUAL SYSTEM

It is a conventional reflex epilepsy, activated by photic stimuli. It may be underlined by any structural lesion. The electrophysiology is a similar burst-firing mode as seen in absence epilepsy[25], based on the cooperation of the pulvinar thalami, the reticular nuclei and the visual cortex. In seizures, visual phenomena appear.

The pulvinar thalami, as a part of the posterior thalamocortical system, participates in the coordination of the visual system during NREM sleep. Experimental studies have shown that visual learning was successful only if a NREM sleep period was involved.

SELF-LIMITING FOCAL CHILDHOOD EPILEPSIES: EPILEPSIES OF THE PERISYLVIAN COMMUNICATION NETWORK (FIG 3)

This is the most prevalent epilepsy spectrum in childhood. It is constituted by conditions occurring between 3 and 14-15 years. A group of them used to be considered benign with no cognitive harm; ceasing by the adolescence. Recently the spectrum has been re-interpreted[27].

The typical interictal discharges of the most common variant Rolandic epilepsy (termed self-limiting epilepsy with centrotemporal spikes - SeLFE- or benign centrotemporal epilepsy), are the centrotemporal spikes distributed bilaterally and independently with a leading hemisphere in most cases. The sensory-motor seizures of the facio-brachial region may generalise; typically in NREM sleep. Interictal and ictal manifestations share the same intrasylvian localisation in the motor strip[28].Interictal discharges are frequent, but seizures are rare and accumulate in NREM sleep. Neuropsychological studies revealed subtle cognitive symptoms in those benign forms, mainly affecting language. A more severe variant of the spectrum is atypical Rolandic epilepsy showing more cognitive loss and atypical EEG symptoms with spike-wave paroxysms. Rarely, opercular status epilepticus may evolve. In the sixties, a malignant and progressive syndrome, electrical status epilepticus in sleep (ESES, recently termed epileptic encephalopathy with continuous spike-wave activity in sleep; EE-SWAS), has also be included in the spectrum[29] often occurring in atypical Rolandic epilepsy children.[29,30] It had been deemed rare affecting just 5-10% of Rolandic epilepsy patients, but recent studies using a more permissive definition of ESES, found its proportion at 30%.[31] In these children, while the awake EEG keeps showing the rare centrotemporal discharges, continuous high voltage discharges- a bilateral 'tsunami 'of spikes and slow waves - cover a substantial part of NREM sleep and blur the borders of sleep stages while leading to the regress of cognitive development[29]. There are reports on successful Sulthiam, ketamine and magnetic stimulation therapies[32]. Several publication reported early intrathalamic haemorrhages in found in those children developed later ESES encephalitis.[33] A rare regional posterior variant of ESES is Landau-Kleffner syndrome, where the Wernicke network is involved resulting in acquired aphasia. These malignant variants typically resist to traditional anti-seizure therapy; they respond to steroids.

The centrotemporal spike parallels the severity of the syndromes across the spectrum. The mildest variants seen in non-epileptic relatives of patients, are single and random sharp waves with no associating ripple; in Rolandic epilepsy, ripples 'crown' centro-temporal spikes, and in the encephalopathic variants, ripple activity increases[34,35].

If the ESES pattern persists for more than 18 months, the regression of mental development may be irreversible. Genetic and minor developmental alterations[36,37] were found in the background of the syndrome.

Reflex epilepsies of the perisylvian communication network

1) Reading epilepsy: a system epilepsy of the brain network for reading[38,39]. In reading induced seizures, the epileptically upregulated reading-network produces ictal myocloni and visual symptoms. To our knowledge, no systematic seep studies have been performed in this group.

2) Musicogenic (and singing, playing music) epilepsy: the epilepsy of the musical communication-system.

   Its seizures are triggered by specific and in most cases, subjectively meaningful music. While the triggering music may be different, the evolving seizures, -typically temporal ones with propagation to the limbic system- may be similar.

Post-injury epilepsies manifest the features of the injured network.

Post-injury epilepsy seems to be a good model of epileptogenesis. The late Mircea Steriade school and its successors have recognised in the sleep EEGs of human post-injury epilepsy, the increase of NREM sleep slow wave down-states and their penetration to both REM sleep and wakefulness. Since the amount of bistable slow oscillations is an accepted measure of sleep homeostatic pressure, the excess of slow wave down states, would suggest the pathological upregulation of homeostasis. Experimental studies[40,41] have revealed the development of paroxysmal activity in those animals with brain-injuries; confirming the link between epilepsy and augmented sleep homeostasis.

Recently a study[44] on stroke patients reported similar enhancement of sleep-like slow wave up - and down - states, but the percentage of epileptic-development in the studied patients is unknown.

To our knowledge, no systematic sleep studies have been performed in post-injury epilepsy either.

The role of NREM sleep in epilepsies

Most epilepsies can be linked to a functional system, and NREM sleep seems to have an essential role.

During epileptogenesis, NREM sleep rhythms transform to interictal epileptic discharges.[19,20] In absence epilepsy, due to a mutation affecting intranuclear GABAergic transmission in the thalamic reticular nucleus, spindle production of NREM sleep may switch to spike-wave production[21].

In epilepsies of the sleep promoting and arousal-systems to and from NREM sleep; seizures are initiated by the activation of the respective brain networks[13].

In a functional MRI study of JME patients falling asleep into NREM, the functional connectivity increased compared to normal controls[42]. In an experimental study in rats, the fractional activation of the sleep-promoting system in waking, could elicit absence-like seizures. Authors suggested that wake-sleep transitions promote absence-activation in genetic rat model[43].

Paralleling the progress of perisylvian epilepsies, NREM sleep-related ripple activity increases[35].In post-injury epilepsies that "model" epileptogenesis, sleep slow wave down states of NREM sleep, intrude also into waking and REM sleep, likely fuelling sleep plasticity[40,41].

Some symptomatologic and taxonomic considerations

The present epilepsy-classification struggles to maintain the focal/generalized dichotomy, while it is increasingly recognized that focal epilepsy is not focal enough and generalized epilepsies present many focal features. The prevailing epilepsy-classification fails also to explain the permanent affinity (togetherness) of manifestations constituting the known epilepsy-syndromes. For example the typical mesiotemporal seizures with acute memory-loss, gastrointestinal and limbic features; the anterior temporal interictal EEG signs; the characteristic

permanent memory deficits as well as hippocampal sclerosis point to the epileptic transformation of the declarative memory-system. The intensive plasticity of this system accounts for MTLE's high prevalence.

Another unclarified issue of the present taxonomy is the spectral belonging of apparently distinct epilepsy conditions, e.g. SeLFE and EE-SWAS, absence epilepsy and juvenile myoclonic epilepsy.

The system-epilepsy approach can resolve these issues and clarify those spectral relations; however, the mechanism and factors of epileptic progression or regression need additional research.

The progress of epilepsy is strongly linked to the notion of secondary epileptogenesis. This is well seen in the dynamic bi-lateralisation-phenomenon in epilepsies typically involving pared-, or midline structures with lateral connections (e.g. mediotemporal lobe epilepsy and hypothalamic hamartomas). These phenomena are obviously related also to the concept of cooperation between the left and right hemisphere (seen among others, in memory functions).

Epilepsies are constituted by chains of dynamic processes. We do not know the exact mechanism of epilepsy induction in a linked, secondary structure (does kindling fully explain this? do chemical or other electric effects have an impact? What is the role of the receiving structure?

In this paper we propose a system-based epilepsy classification, which may provide opportunities to clarify several now unresolved issues.

All these issues are related to the epileptic upgrading process by which a normally functioning brain network may turn to an epileptic working mode.

Future lines of research

We propose to use sleep EEG not just as a diagnostic tool; rather, as an observation-device of the hidden epileptic transformation. Of course, this approach needs a systematic methodological workup including the creation of a normative data-store of sleep grapho-elements, especially during periods of development. Artificial intelligence and spread of long-term home video-EEG monitoring could help.

Summary

In this brief review we aimed to present the development of sleep-research about the homeostatic regulation of NREM sleep and synaptic plasticity. These data alighting sleep as cradle of human cognitive development have importantly impacted on epilepsy research as well. Most importantly, epileptogenesis is seen as an inbuilt risk; the derailment in homeostatic plasticity. This approach goes hand in hand with the emerging system- concept of epilepsies abolishing the "Procrustean bed" of the forced focal- generalized epilepsy-concept. Based on the system concept, we apply the system-approach and briefly reinterpret the most frequent epilepsies that are underlined by different aetiologies but shared mechanisms; and suggest a need of a new taxonomy.

References:

1. Borbély AA. A two process model of sleep regulation. Hum Neurobiol. 1982;(3):195-204.

2. Tononi G, Cirelli C. Sleep and synaptic homeostasis: a hypothesis. Brain Res Bull. 2003;62 (2):143-50. doi: 10.1016/j.

3. Tononi G, Cirelli C. Sleep function and synaptic homeostasis. Sleep Medicine Reviews 2006; 10(1): 49-62. https://doi.org/10.1016/j.smrv.2005.05.002

4. Kattler H, Dijk DJ, Borbély AA. Effect of unilateral somatosensory stimulation prior to sleep on the sleep EEG in humans. J Sleep Res 1994;3: 159–64.

5. **Tononi G, Cirelli C.** Sleep and the price of plasticity: from synaptic and cellular homeostasis to memory consolidation and integration. Neuron. 2014 Jan 8;81(1):12-34. doi: 10.1016/j.neuron.2013.12.025

6. Buzsáki Gy, Bayardo F, Miles R, Wong RKS, Gage FH. The grafted hippocampus: An epileptic focus. Experimental Neurology. 1989; 105 (1):10-22. https://doi.org/10.1016/0014-4886(89)90167-2

7. Goddard GV, McIntyre DC, Leech CK. A permanent change in brain function resulting from daily electrical stimulation. Exp Neurol. 1969;25(3): 295-330. doi: 10.1016/0014-4886(69)90128-9.

8. Beenhakker MP, Huguenard JR. Neurons that fire together also conspire together: is normal sleep circuitry hijacked to generate epilepsy? Neuron. 2009;11;62(5):612-32. doi: 10.1016/j.neuron.2009.05.015.

9. Nobili L, Frauscher B, Eriksson S, Gibbs SA, Halasz P, Lambert I, Manni R, Peter-Derex L, Proserpio P, Provini F, de Weerd A, Parrino L. Sleep and epilepsy: A snapshot of knowledge and future research lines. J Sleep Res. 2022;31(4):e13622. doi: 10.1111/jsr.13622

10. Frauscher B, Gotman J. Sleep, oscillations, interictal discharges, and seizures in human focal epilepsy. Neurobiol Dis. 2019;127:545-53. doi: 10.1016/j.nbd.2019.04.007.

11. Sheybani L, Frauscher B, Bernard C, Walker MC. Mechanistic insights into the interaction between epilepsy and sleep. Nat Rev Neurol. 2025;21(4): 177-92. doi: 10.1038/s41582-025-01064-z.

12. Bernard C, Frauscher B, Gelinas J, Timofeev I. Sleep, oscillations and epilepsy. Epilepsia. 2023;64 Suppl 3(Suppl 3):S3-12. doi: 10.1111/epi.17664

13. Halász P, Szűcs A. Sleep and epilepsy, link with plasticitY Front Neurol. 2020 Aug 28;11:911. doi: 10.3389/fneur.2020.00911.

14. Maglóczky Z, Freund TF. Selective neuronal death in the contralateral hippocampus following unilateral kainate injections into the CA3 subfield. Neuroscience. 1993;56(2):317–336. doi: 10.1016/0306-4522(93)90334-c.

15. Avanzini G, Manganotti P, Meletti S, Moshé SL, Panzica F, Wolf P, Capovilla G. The system epilepsies: a pathophysiological hypothesis. Epilepsia. 2012;53(5):771-8. doi: 10.1111/j.1528-1167.2012.03462.x.

16. Wolf P, Yacubian EM, Avanzini G, Sander T, Schmitz B, Wandschneider B, Koepp M. Juvenile myoclonic epilepsy: A system disorder of the brain. Epilepsy Res. 2015;114:2-12. doi: 10.1016/j.epilepsy res.2015.04.008.

17. Striano P, Striano S. Reading epilepsy and its variants: a model for system epilepsy. Epilepsy Behav. 2011;20(3):591. doi: 10.1016/j.yebeh.2011.01.021

18. Halász P, Kelemen A, Clemens B, Saracz J, Rosdy B, Rásonyi G, Szücs A. The perisylvian epileptic network. A unifying concept. Ideggyogy Sz. 2005; 58(1-2):21-31.

19. Buzsáki G. Hippocampal Sharp Wave-Ripple: A cognitive Biomarker for Episodic Memory and Planning. Hippocampus. 2015;25–8, 10738 10.1093/brain/awaa072.

20. Gulyás A, Freund T. Physiological and pathological high frequency oscillations: The role of perisomatic inhibition in sharp-wave ripple and interictal spike generation10.1126/science.8392750. Current Opinion in Neurobiology. 2015; 31:26–32.

21. von Krosigk M, Bal T, McCormick DA. Cellular mechanisms of a synchronized oscillation in the thalamus. Science. 1993, 16;261(5119):361-4. doi:

22. Crunelli V, Lőrincz ML, McCafferty C, Lambert RC, Leresche N, Di Giovanni G, David F. Clinical and experimental insight into pathophysiology, comorbidity and therapy of absence seizures. Brain. 2020;143(8):2341-2368. doi.

23. Hayman M, Scheffer IE, Chinvarun Y, Berlangieri SU, Berkovic SF. Autosomal dominant nocturnal frontal lobe epilepsy: demonstration of focal frontal onset and intrafamilial variation. Neurology. 1997;49(4):969-75. doi: 10.1212/wnl.49.4.969.

24. Halasz P, Simor P,Szűcs A. Fearful arousals in sleep terrors and sleep-related hypermotor epilepticseizures may involve the salience network and the acute stress response of Cannon and Selye Epilepsy Behav Rep. 2024 Feb 1;25:100650. doi:10.1016/j.ebr.2024.100650.

25. Durkin J, Aton SJ. Sleep-Dependent Potentiation in the Visual System Is at Odds with the Synaptic Homeostasis Hypothesis, Sleep, 2016; 19:155– https://doi.org/10.5665/sleep.5338

26. Schomers MR, Garagnani M, Pulvermüller F. Neurocomputational consequences of evolutionary connectivity changes in perisylvian language cortex. J Neuroscience. 2017;37(11):3045–55. https://doi.org/10.1523/jneurosci.2693-16.2017

27. Specchio N, Wirrell EC, Scheffer IE, Nabbout R, Riney K, Samia P, Guerreiro M, Gwer S, Zuberi SM, Wilmshurst JM, Yozawitz E, Pressler R, Hirsch E, Wiebe S, Cross HJ, Perucca E, Moshé SL, Tinuper P, Auvin S. International League Against Epilepsy classification and definition of epilepsy syndromes with onset in childhood: Position paper by the ILAE Task Force on Nosology and Definitions. Epilepsia. 2022; 63:1398–442. doi: 10.1111/epi.17241

28. Alving, J., Fabricius, M., Rosenzweig, I., & Beniczky, S. (2017). Ictal source imaging and electroclinical correlation in self-limited epilepsy with centrotemporal spikes. *Seizure - European Journal of Epilepsy*, *52*, 7-10. https://doi.org/10.1016/j.seizure.2017.09.006

29. Tassinari CA, Cantalupo G, Rios-Pohl L, Giustina ED, Rubboli G. Encephalopathy with status epilepticus during slow sleep: "the Penelope syndrome". Epilepsia. 2009;50 Suppl 7:4-8. doi: 10.1111/j.1528-1167.2009.02209.x.

30. Halász P, Szűcs A. Self-limited childhood epilepsies are disorders of the perisylvian communication system, carrying the risk of progress to epileptic encephalopathies-Critical review. Front Neurol. 2023; 1: 1092244. doi: 10.3389/fneur.2023.1092244.

31. Lu G, Cheng Y, Yang W, Hu J, Zhang F. The Prevalence and Risk Factors of Electrical Status Epilepticus During Slow-Wave Sle Clin EEG Neurosci. 2024; 55(2):265-271. https://doi.org/10.1177/15500594231182758

32. Posar A, Visconti P. Continuous Spike-Waves during Slow Sleep Today: An Update. Children (Basel). 2024;11(2):169. doi: 10.3390/children11020169.

33. an den Munckhof B, Zwart AF, Weeke LC, Claessens NHP, Plate JDJ, Leemans A, Kuijf HJ, van Teeseling HC, Leijten FSS, Benders MJN, Braun KPJ, de Vries LS, Jansen FE. Perinatal thalamic injury: MRI predictors of electrical status epilepticus in sleep and long-term neurodevelopment. Neuroimage Clin. 2020;26:102227. doi: 10.1016/j.nicl.2020.102227

34. Kobayashi K, Yoshinaga H, , Toda Y, Inoue T, Oka M. High-frequency oscillations in idiopathic partial epilepsy of childhood. Epilepsia 2011; 52(10):p. 1812-9; https://doi.org/10.1111/j.1528-1167.2011.03169.x

35. van Klink NE, van 't Klooster MA, Leijten FS, Jacobs J, Braun KP, Zijlmans M. Ripples on rolandic spikes: A marker of epilepsy severity. Epilepsia. 2016; 57:1179–89. 10.1111/epi.13423

36. Overvliet GM, Besseling RM, Vles JS, Hofman PA, Backes WH, van Hall MH, Klinkenberg S, Hendriksen J, Aldenkamp AP. Nocturnal epileptiform EEG discharges, nocturnal epileptic

seizures, and language impairments in children: review of the literature. Epilepsy Behav. 2010;19 (4):550-8. doi: 10.1016/j.yebeh.2010.09.015.

37. Vaudano AE, Avanzini P, Cantalupo G, Filippini M, Ruggieri A, Talami F, Caramaschi E, Bergonzini P, Vignoli A, Veggiotti P, Guerra A, Gessaroli G, Santucci M, Canevini MP, Piccolo B, Pisani F, Gobbi G, Dalla Bernardina B, Meletti S. Mapping the Effect of Interictal Epileptic Activity Density During Wakefulness on Brain Functioning in Focal Childhood Epilepsies With Centrotemporal Spikes. Front Neurol. 2019;10:1316. doi: 10.3389/fneur.2019.01316.

38. Wolf P. Reading epilepsy. In: Roger J, Bureau M, Dravet C, Dreifuss FE, Perret A, Wolf P, ed. Epileptic syndromes in infancy, childhood and adolescence. 2nd ed. London: John Libbey, 1992: 281-98.

39. Puteikis K, Mameniškienė R, Wolf P. Reading epilepsy today: A scoping review and meta-analysis of reports of the last three decades. Epilepsy Behav. 2023;145:109346. doi: 10.1016/j.yebeh.2023.109346.

40. Timofeev I, Bazhenov M, Avramescu S, Nita DA. Posttraumatic epilepsy: the roles of synaptic plasticity. Neuroscientist. 2010;16(1):19-27. doi: 10.1177/1073858409333545.

41. Houweling AR, Bazhenov M, Timofeev I, Steriade M. Sejnowski TJ. Homeostatic Synaptic Plasticity Can Explain Post-traumatic Epileptogenesis in Chronically Isolated Neocortex Cerebral Cortex 2005; 15(6): 83-45
https://doi.org/10.1093/cercor/bhh184

42. Bagshaw AP, Rollings DT, Khalsa S, Cavanna AE. Multimodal neuroimaging investigations of alterations to consciousness: the relationship between absence epilepsy and sleep. Epilepsy Behav. 2014;30:33-7. doi:0.1016/j.yebeh.2013.09.027

43. Suntsova N, Kumar S, Guzman-Marin R, Alam MN, Szymusiak R, McGinty D. A role for the preoptic sleep-promoting system in absence epilepsy. Neurobiol Dis. 2009 Oct;36(1):126-41. doi: 10.1016/j.nbd.2009.07.005.

44. Massimini M, Corbetta M, Sanchez-Vives MV, Andrillon T, Deco G, Rosanova M, Sarasso S. Sleep-like cortical dynamics during wakefulness and their network effects following brain injury. Nat Commun. 2024;15(1):7207. doi: 10.1038/s41467-024-1586-1

