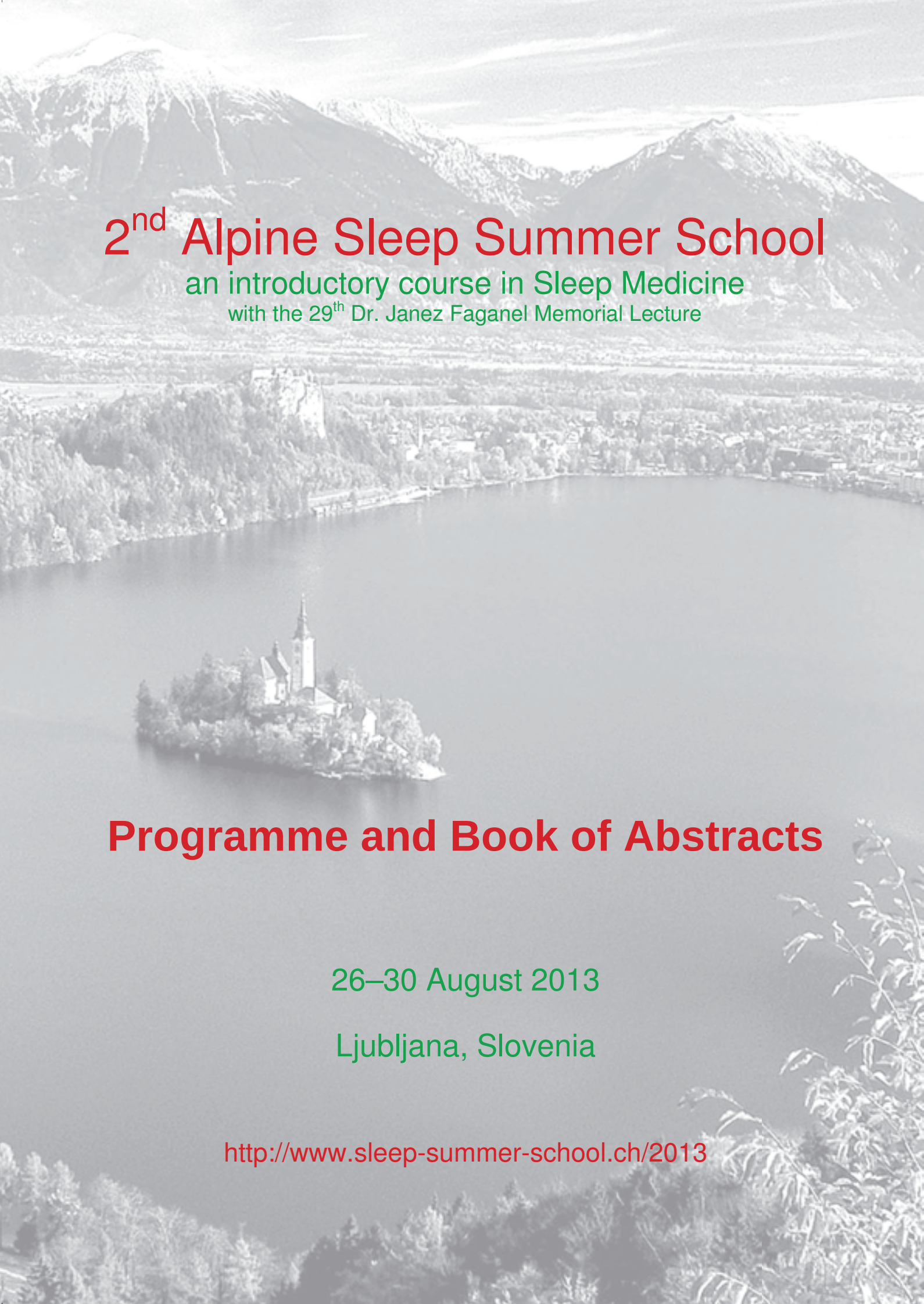

2nd Alpine Sleep Summer School

an introductory course in Sleep Medicine

with the 29th Dr. Janez Faganel Memorial Lecture

Programme and Book of Abstracts

26–30 August 2013

Ljubljana, Slovenia

http://www.sleep-summer-school.ch/2013

2nd Alpine Sleep Summer School

an Introductory Course in Sleep Medicine

with the 29th Dr. Janez Faganel Memorial Lecture

Organised by:

Section for Clinical Neurophysiology of the Slovenian Medical Association

and

Institute of Clinical Neurophysiology, Division of Neurology
of the University Medical Centre Ljubljana

Endorsed by:

European Sleep Research Society – ESRS

and

ERS EUROPEAN RESPIRATORY SOCIETY

Technical Organiser:

Congress Centre *Cankarjev dom* Ljubljana

26–30 August 2013
Grand Hotel Union, Ljubljana, Slovenia

The 2nd ASSS was granted **30 European CME credits** (ECMEC)
by the European Accreditation Council for Continuing Medical Education (EACCME)

Programme and Book of Abstracts

2nd Alpine Sleep Summer School
an Introductory Course in Sleep Medicine
with the 29th Dr. Janez Faganel Memorial Lecture

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COMMITTEES

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WELCOME ADDRESS

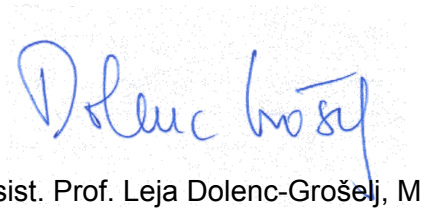
Dear Colleagues and Guests

We are pleased that the 2nd Alpine Sleep Summer School (ASSS) will take place in Ljubljana, one of the most charming cities in the Central Europe, the capital of Slovenia, small and young European country on the sunny side of the Alps. Ljubljana, at a crossroads between the East and West of Europe, with its unique historical atmosphere, very active cultural and academic life, as well as with a moderate climate, is a unique place for the summer school.

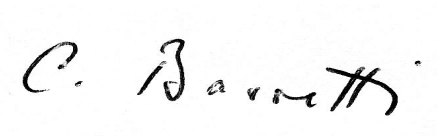
The first Sleep School took place in Lugano, Switzerland, in the summer 2011. The aim of the ASSS is to offer in the Central ("Alpine") Europe a state of the art introduction into sleep medicine to students, MDs, PhDs, technicians, and other health and scientific professionals involved or interested in sleep medicine. The School extends over 5 days, each of which is covering the main topics (*basics of sleep* on Monday, *sleep and psychiatry* on Tuesday, *sleep and respiratory medicine* on Wednesday, *sleep and neurology* on Thursday, and *sleep and paediatrics* on Friday). The programme consists of 5 special lectures, one of them the so called Dr. Janez Faganel Memorial Lecture of generally local tradition and importance, on "hot topics" in sleep medicine and sleep research, of 30 lectures, 25 practical sessions, many of them case studies presented by video clips.

On behalf of the Organising and Scientific Committee we are grateful to build on the success and experience of the 1st ASSS, including our main sponsors Respironics and UCB.

We warmly welcome you to the 2nd Alpine Sleep Summer School in Ljubljana.



Asist. Prof. Leja Dolenc-Grošelj, MD, PhD



Prof. Claudio L. Bassetti, MD, PhD

2nd Alpine Sleep Summer School (ASSS)

an introductory course in Sleep Medicine

http://www.sleep-summer-school.ch/2013

26 - 30.08.2013
Ljubljana, Slovenia

	Monday August 26, 2013	**Tuesday** August 27, 2013	**Wednesday** August 28, 2013	**Thursday** August 29, 2013	**Friday** August 30, 2013
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	Monday August 26, 2013	Tuesday August 27, 2013	Wednesday August 28, 2013	Thursday August 29, 2013	Friday August 30, 2013
Lecture ***Coordinators***	**Sleep, Basics** **Dolenc-Groselj/Dogas**	**Sleep and Psychiatry** **Pollmächer/Manconi**	**Sleep and Respiratory Medicine** **Penzel/Högl**	**Sleep and Neurology** **Ferini-Strambi/Mathis**	**Sleep and Pediatrics** **Kerbl/Bruni**
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GENERAL INFORMATION

Registration Fees

Participants	600 €
Students	450 €

Congress Fees Include

- Participation in the Summer School
- Conference materials
- Thirty (30) European CME credits (ECMEC)
- Two coffee breaks per day (26–30 August)
- Lunch (26–30 August)
- Evening Cultural Event on 27 August
- Sightseeing of Bled & Conference Dinner on 29 August

Venue

Grand Hotel Union, Miklošičeva cesta 1, Ljubljana

- Registration: in front of the White Hall
- Sessions: White Hall
- Exhibition & Breaks: Garden Hall
- Lunch: Restaurant of the Grand Hotel Union

Social Programme (included in the participant's fee, name badges obligatory)

Tuesday, 27 August

20:00–23:00 Evening Cultural Event, B&B Slamič, 1 Kersnikova Street, Ljubljana
Meeting point: 19:45 at the Grand Hotel Union Business/Reception Desk (5-minute walking distance)

Thursday, 29 August – *hosted by Philips Respironics*

18:00–23:00 Sightseeing of Bled & Conference Dinner
Meeting point: 18:00 at Grand Hotel Union Business/Reception Desk
Departure time: 18:15 (by bus)

Accompanying Person's Programme

- Ljubljana sightseeing walking tour (2 hours) on August 28, 2013 (10:00–12:00); price per person: 12.80 €

Accompanying persons are welcome to join the social events:

- Evening Cultural Event on 27 August; price: 20.00 €
- Sightseeing of Bled & Conference Dinner on 29 August; price: EUR 50.00 €

TECHNICAL INFORMATION

Registration and Information Desk

The Registration Desk for the ASSS Conference will be located in front of the White Hall, Grand Hotel Union Executive, and will open as follows:

Sunday, 25 August	17:00–19:00
Monday, 26 August	8:00–18:00
Tuesday, 27 August	8:00–12:00
Wednesday, 28 August	8:00–12:00
Thursday, 29 August	8:00–12:00

Conference Identification Badge

A conference identification badge will be included in the conference material provided upon Registration. There will be no admittance to the Scientific Sessions and Social Events without the conference badge.

- During session breaks, refreshments will be served free of charge to participants wearing congress badges.
- Working lunches are included in the registration fee and will be served at lunchtime in the Restaurant of Grand Hotel Union.
- The official language of the Conference is English.
- A Certificate of Attendance will be issued to all registered participants.

ABSTRACTS/NOTES

1

Neurobiology of wake, SWS, REM sleep

Pierre-Hervé Luppi[1,2,3]

[1]*Lyon Neuroscience Research Center, Team Physiopathologie des réseaux neuronaux du cycle veille-sommeil, Lyon, France*

[2]*University of Lyon, Lyon, France*

[3]*University Claude Bernard Lyon 1, Lyon, France*

Since the discovery of rapid eye movement (REM) sleep (also known as paradoxical sleep; PS), it is accepted that sleep is an active process. PS is characterised by EEG rhythmic activity resembling that of waking with a disappearance of muscle tone and the occurrence of REMs, in contrast to slow-wave sleep (SWS, also known as non-REM sleep) identified by the presence of delta waves. I will describe an updated integrated model of the mechanisms responsible for the sleep-wake cycle. This model is based on results showing that the switch between waking and SWS is under the control of reciprocal interconnections between a population of SWS-active neurons located in the preoptic area and multiple waking systems. This model also introduces the notion that the entrance and exit of PS are induced by different mechanisms. I will hypothesize that the entrance from SWS to PS is due to the intrinsic activation of PS-on GABAergic neurons. These populations of neurons would inhibit during PS all waking systems and a population of PS-off GABAergic neurons. This population of PS-off GABAergic neurons tonically inhibits during waking and SWS the glutamatergic neurons triggering the state of PS localized in the pontine sublaterodorsal tegmental nucleus (SLD). The exit from PS would be induced by the inhibition of the PS-on GABAergic neurons by waking systems such as the pontine and medullary noradrenergic neurons and the hypothalamic hypocretin.

Notes

2

Neurochemistry of sleep-wake systems

Hans-Peter Landolt[1,2]

[1]*Institute of Pharmacology & Toxicology, University of Zürich, Zürich, Switzerland*

[2]*Zürich Center for inter-disciplinary Sleep Research (ZiS), University of Zürich, Zürich, Switzerland*

This lecture will review the concepts and some recent findings, which contributed to our current understanding of the brain circuitry and the neurotransmitters that regulate the daily cycles of wakefulness and sleep. Wakefulness is promoted by hypothalamic and brain stem neurons producing hypocretin, histamine, noradrenaline, serotonin, dopamine, and acetylcholine. Co-ordinated activity in these distinct neuronal groups activates thalamus and cerebral cortex by a ventral pathway (aminergic) and a dorsal pathway (cholinergic), to ensure full alertness and cortical activation. Rapid-eye-movement (REM) sleep and non-rapid-eye-movement (non-REM) sleep are controlled by cholinergic neurons in the pons, and γ-amino-butyric acid (GABA) and galanin containing neurons in ventro-lateral pre-optic area of the hypothalamus. Mutual interactions among these wake- and sleep-promoting regions likely permit to maintain consolidated periods of wakefulness and sleep. Sleep architecture and non-REM sleep intensity are further modulated by the endogenous circadian clock, as well as the prior duration and the quality of wakefulness. Genetically determined differences in the neurochemical mechanisms underlying synaptic plasticity contribute to robust inter-individual differences in sleep intensity in humans.

Notes

3

Circadian regulation of sleep and light

Christian Cajochen

Centre for Chronobiology, University of Basel, Basel, Switzerland

All of our behaviours are influenced or regulated by endogenous clocks, a major one, being the circadian (i.e. about a day) clock. Strategically optimally located in the suprachiasmatic nuclei of the anterior hypothalamus, this clock receives light information via the retinohypothalamic tract directly from the retina's classical and non-classical photoreceptors. This light input is crucial, since circadian rhythms need to entrained to the precise 24-h solar day. Thus, most living organisms have adapted their temporal organization of behaviour and physiology to optimally anticipate the 24-h light dark cycle on Earth.

Sleep-wake behaviour is a major "behaviour output", which is regulated by the circadian clock – a fact most clinicians working in the field of sleep medicine are not aware of. This is rather surprising, since surveys on the causes of sleep problems rank circadian sleep disturbances under the top 3 most commonly reported sleep complaints in Germany. Light impacts our circadian rhythms more powerfully than any drug. Beyond vision, light has other physiological effects through sightless vision. It inhibits sleep-promoting hypothalamic brain areas and activates arousal-promoting orexin neurons in the hypothalamus, and attenuates the nightly release of the soporific hormone melatonin. These factors reduce sleepiness, increase alertness and performance for higher cognitive tasks and interfere with our sleep.

I will highlight the importance of circadian sleep regulation and the impact of light on sleep, neuroendocrine, alerting and neurocognitive responses. These effects are far more complex and nuanced than initially thought. The aim is to increase our awareness of the importance of both natural and artificial light for human health and well-being.

Notes

4

Homeostatic regulation of sleep

Peter Achermann

University of Zürich, Institute of Pharmacology and Toxicology, Zürich, Switzerland

Sleep homeostasis denotes a salient aspect of sleep regulation. Non-rapid eye movement (non-REM) sleep pressure builds up during the day and dissipates across the night. A sleep deficit results in prolongation and intensification of sleep at the next sleep opportunity. An important physiological marker of non-REM sleep pressure is EEG spectral power in the delta band (sleep EEG power between 0.5 and 4.5 Hz), called slow-wave activity (SWA). SWA shows a rebound following sleep deprivation proportional to the amount of sleep lost. Moreover, the decline in SWA across the night can be fit with an exponential decay function and reflects the dissipation of sleep pressure. Less is known about REM sleep homeostasis, in part due to the absence of known physiological markers of REM sleep intensity. Sleep pressure is also reflected in the waking EEG. The study of sleep homeostasis has potential for providing insights into the functions of sleep and individual differences in sleep regulation.

Notes

5

Genetic determinants of sleep-wake regulation

Hans-Peter Landolt[1,2]

[1]*Institute of Pharmacology & Toxicology, University of Zürich, Switzerland*

[2]*Zürich Center for inter-disciplinary Sleep Research (ZiS), University of Zürich, Switzerland*

The contribution of slow brain oscillations including delta, theta, alpha and sigma frequencies (0.5–16 Hz) to the sleep EEG is finely regulated by circadian and homeostatic influences, and reflects functional aspects of wakefulness and sleep. Accumulating evidence demonstrates that individual sleep EEG patterns in non-rapid-eye-movement (non-REM) sleep and rapid-eye-movement (REM) sleep are heritable traits. More specifically, multiple recordings in the same individuals, as well as studies in monozygotic and dizyogotic twins suggest that a very high percentage of the robust inter-individual variation and the high intra-individual stability of sleep EEG profiles can be explained by genetic factors (> 90% in distinct frequency bands). Still little is known about which genes contribute to different sleep EEG phenotypes in healthy humans. The genetic variations that have been identified to date include functional polymorphisms of the clock gene PER3, and of genes contributing to signal transduction pathways involving adenosine (ADA, ADORA2A), dopamine (DAT, COMT), glutamate (FMR1), brain-derived neurotrophic factor (BDNF), and prion protein (PRNP). Some of these polymorphisms profoundly modulate sleep EEG profiles; their effects will be reviewed in this lecture. The search for genetic contributions to slow sleep EEG oscillations constitutes a promising avenue to identify molecular mechanisms underlying sleep-wake regulation in humans.

Notes

6

Sleep and respiratory control

Zoran Dogas

University of Split, School of Medicine, Department of Neuroscience, Split, Croatia

There is solid evidence showing that the neural networks involved in state control are tightly connected to respiratory-related areas and/or to respiratory neurons, and the changes affecting these networks during the sleep/wake cycle may also affect the control of breathing. A specific depresssion of minute ventilation occurs during sleep in normal subjects. This sleep-related ventilatory depression is partially related to mechanical events and upper airway atonia but some data also indicate that it is likely to be centrally mediated. The sleep-related ventilatory depression depends upon the enhanced GABAergic activity together with a loss of suprapontine influence depending on the cessation of activity of the reticular formation.

Plasticity of the nervous system is a basis of many physiological functions such as learning and memory. It is defined as permanent change in the nervous control system based on previous experience. Respiratory control system also posses an impressive plasticity which may be defined as a long term change of respiratory pattern when original stimulus is not present any more. Respiratory plasticity may be induced by hypoxia, hypercapnia, exercise, injury or stress. Plasticity of the respiratory system includes two forms induced by intermittent hypoxia: carotid chemosensitive plasticity following chronic intermittent hypoxia, and long term facilitation (LTF) of respiratory motor output following acute intermittent hypoxia (AIH).

LTF of breathing, often seen as phrenic LTF, is central (or spinal) neural mechanism that exhibits prolonged increase of respiratory motor output following episodes of AIH. It lasts long after direct effects of hypoxia. Hypoxia stimulates carotid chemoreceptors, which then in turn activate respiratory neurons in medulla (responsible for rhythm) and 5-HT neurons in raphe nuclei. Released 5-HT from raphe terminals activates serotonin receptors on phrenic motoneurons. This mechanism is very sensitive to anaesthetics, serotonin, and opioide drugs.

So far, there were unsuccessful tries to evoke it in awake humans but it was observed during non-REM sleep. LTF is considered to be a useful factor in maintenance of respiratory homeostasis during sleep, which may increase the muscle tone of upper airways. It is, therefore, suggested that LTF is an early defence mechanism in obstructive sleep apnea patients.

There is another mechanism of neuronal output control called gain modulation that was observed on respiratory pre-motor neurons, which may play an important role in shaping the respiratory pattern. This mechanism is presumably mediated by GABAA receptors and could be seen following the central administration of their antagonist bicuculline.

Further studies of these central neuronal mechanisms of respiratory control may provide new insights into our present knowledge of respiratory disturbances during sleep and may lead us to better diagnostic and therapeutic approaches for a very large patient population in this field of sleep medicine.

Notes

7 – Special lecture
29th Dr. Janez Faganel Memorial Lecture

State of the neuronal network responsible for paradoxical (REM) sleep in neurological disorders?

Pierre-Hervé Luppi[1,2,3]

[1]*Lyon Neuroscience Research Center, Team Physiopathologie des réseaux neuronaux du cycle veille-sommeil, Lyon, France*

[2]*University of Lyon, Lyon, France*

[3]*University Claude Bernard Lyon 1, Lyon, France*

Since the discovery of rapid eye movement (REM) sleep (also known as paradoxical sleep; PS), it is accepted that sleep is an active process. PS is characterised by EEG rhythmic activity resembling that of waking with a disappearance of muscle tone and the occurrence of REMs, in contrast to slow-wave sleep (SWS, also known as non-REM sleep) identified by the presence of delta waves. I will describe an updated integrated model of the mechanisms responsible for REM sleep genesis. This model introduces the notion that the entrance and exit of PS are induced by different mechanisms. I will hypothesize that the entrance from SWS to PS is due to the intrinsic activation of PS-on GABAergic neurons. These populations of neurons would inhibit during PS all waking systems and a population of PS-off GABAergic neurons. This population of PS-off GABAergic neurons tonically inhibits during waking and SWS the glutamatergic neurons triggering the state of PS localized in the pontine sublaterodorsal tegmental nucleus (SLD). The exit from PS would be induced by the inhibition of the PS-on GABAergic neurons by waking systems such as the pontine and medullary noradrenergic neurons and the hypothalamic hypocretin. Finally, I will propose hypotheses on the mechanisms responsible for two main sleep pathologies, REM sleep behaviour disorder and narcolepsy.

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Notes

8 – Practical session

Approach to sleep-wake disorders – Sleep questionnaires

Leja Dolenc-Grošelj

Institute of Clinical Neurophysiology, University Medical Center Ljubljana, Ljubljana, Slovenia

The evaluation of a patient with disordered sleep begins with the chief complaint, which can be classified into insomnia, daytime sleepiness, episodic nocturnal movements or behaviours, or a combination of these concerns. A thorough characterization of these concerns, coupled with a comprehensive sleep history that includes the daily schedule, bedtime routine, and morning and daytime symptoms, forms the foundation for diagnosis. Ideally, the evaluation includes a history from the patient's bed partner. It is essential to consider other medical and psychiatric conditions, medication use, family history, social history including the psychosocial situation, review of systems, and physical examination before formulating a differential diagnosis and performing diagnostic studies. This systematic approach allows accurate diagnosis and specific interventions for many treatable sleep disorders. Diagnosis of sleep disorder should always be made on the basis of the *International Classification of Sleep Disorders* (ICSD-2). On the basis of the relative likelihood of the diagnostic possibilities, appropriate diagnostic studies are ordered. Even when the diagnosis is clear, laboratory tests may be required to determine the severity of the condition before the clinician decides on the appropriate treatment. Additional diagnostic information can be obtained through the use of laboratory or radiologic investigations, sleep logs, sleep questionnaires and sleep laboratory studies. The sleep log is particularly useful in patients with insomnia or suspected circadian rhythm disturbances. Regarding the type of sleep disorder different sleep questionnaires can be used. The Pittsburgh Sleep Quality Index (PSQI) is a self-rated questionnaire which assesses sleep quality and disturbances over a 1-month time interval. The Berlin Questionnaire is a simple sleep apnoea screening questionnaire used to quickly identify the risk (low to high) of sleep disordered breathing. Questionnaires such as Epworth Sleepiness Scale and the Stanford Sleepiness scale provide a reliable measure of excessive daytime sleepiness. Circadian chronotype questionnaires, such as Horne-Östberg Morningness-Eveningness Questionnaire (MEQ) and Basic Language Morningness (BALM) scale, are used for screening of circadian disorders. Polysomnography can provide confirmatory diagnostic evidence in cases of sleep apnea, narcolepsy, periodic limb movements, nocturnal seizures, and sleep terrors and helps determine the severity of these conditions. Its use in the evaluation of insomnia is somewhat controversial but may be beneficial, especially when sleep apnea, periodic limb movements, or sleep state misperception is suspected. For objective diagnosis of excessive daytime sleepiness, variations of the *Multiple Sleep Latency Test* and other physiological tests can be used.

Sleep disorders are prevalent in the general population. Patients with complaints of sleep disturbance often present a diagnostic challenge to the clinician because of the many possible causes of symptoms. A systematic evaluation usually leads to a provisional diagnosis or a set of diagnostic possibilities that can be confirmed or excluded with specific diagnostic tests. With accurate diagnosis and specific interventions, most sleep disorders are treatable.

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Notes

9 – Practical session

Actigraphy / Polygraphy

Zoran Dogas

University of Split, School of Medicine, Department of Neuroscience, Split, Croatia

Actigraphy is a valid way to assess sleep-wake patterns in patients suspected of certain sleep disorders, but the method cannot fully be a substitute for polygraphy or polysomnography.

The term actigraphy refers to methods using miniaturised computerised wrist watch-like devices to monitor and collect data generated by movements. Most actigraphs contain an analogue system to detect movements. In some devices, a piezo-electric beam detects movement in two or three axes and the detected movements are translated to digital counts accumulated across pre-designed epoch intervals (e.g. 1 min) and stored in the internal memory. The actigraph can collect data continuously over an extended period (1 week or longer). Some devices are programmable and enable selection of specific modes of operation (e.g. variable movement frequency bandwidths, sensitivity levels or epoch intervals) whereas other devices have only one fixed mode. Data are downloaded to the computer using special interface units or other forms of communication channels. The use of computer scoring algorithms without controlling for potential artifacts can lead to inaccurate or misleading results.

Actigraphy is commonly used in patients suspected of advanced sleep phase syndrome (ASPS), delayed sleep phase syndrome (DSPS) or shift work sleep disorder. It can also be indicated in circadian rhythm disorders including jet lag and non 24-hour sleep/wake syndrome including that associated with blindness. However, since actigraphic rest-activity patterns cannot provide an undisputable marker of circadian timing, circadian rhythm assessment (e.g. melatonin, core body temperature, cortisol) is useful for diagnosis. Currently the timing of the melatonin rhythm (e.g. time of melatonin onset) is considered the most reliable marker of circadian phase.

In patients with insomnia (including those with depression), excessive daytime sleepiness/hypersomnia (including those with behaviourally induced sleep insufficiency syndrome), or sleep-related movement disorders, actigraphy can be of additional diagnostic value.

Polygraphy (portable monitoring). The standard approach to diagnosing OSA is in-laboratory, technician-attended, polysomnography. Portable monitoring (PM) has been proposed as a substitute for polysomnography in the diagnostic assessment of patients with suspected OSA. PM requires less technical expertise, is less labor intensive and time consuming, and is easier for patients to access. The term portable monitoring encompasses a wide range of devices that can record as many signals as does attended polysomnography or only 1 signal, such as oximetry.

Polygraphy (PG) has four to eight channels of physiological data, but EEG is not recorded. The minimum set of channels comprises O_2-saturation, airflow, breathing effort, heart rate, and body position. It is particularly useful for the diagnosis of obstructive sleep apnea without significant co-morbid condition. It is not useful for the diagnosis of other sleep disorders. It has to be performed by trained and certified medical sleep specialists. Manual scoring is mandatory. Equivocal test results require the subsequent performance of full polysomnography as a standard practice. The final outcome is a report as described in the European Guidelines for Accreditation of SMCs.

The workload comprises admitting the patient by the medical specialist, and preparation of the equipment, patient hook-up, and scoring of the record are performed by the sleep technician. The sleep expert subsequently reviews the scoring, creates the report, and gives feedback to the patient. Attended PG requires continuous monitoring by trained technical and nursing staff for the duration of recording.

Notes

10 – Practical session

PSG-scoring: rules and pitfalls

Leja Dolenc-Grošelj

Institute of Clinical Neurophysiology, University Medical Center Ljubljana, Ljubljana, Slovenia

Five years have passed since the American Academy of Sleep Medicine (AASM) published *The AASM Manual for the Scoring of Sleep and Associated Events*. The manual represents a brave effort to standardize how a comprehensive in-laboratory polysomnogram (PSG) should be recorded, scored, analyzed, and reported. Based on digital video-PSG recording techniques, the manual incorporates the effects of age and disease on sleep and provides rules for visual scoring of sleep stages, arousals, movements, respiratory and cardiac events during sleep.

The greatest criticism has been directed at the AASM's respiratory rules. Therefore the American Academy of Sleep Medicine (AASM) Sleep Apnea Definitions Task Force reviewed the rules for scoring respiratory events. The task force made recommendations concerning recommended and alternative sensors for the detection of apnea and hypopnea, scoring of apneas, hypopneas and hypoventilation.

Detailed PSG scoring rules on the basis of *AASM Manual for the Scoring of Sleep and Associated Events* will be presented. Different PSG cases in adults will be shown and pitfalls in PSG scoring rules will be discussed.

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Notes

11 – Practical session

Quantitative methods of sleep evaluation

Peter Achermann

University of Zürich, Institute of Pharmacology and Toxicology, Zürich, Switzerland

The EEG is a complex signal and an important brain state indicator (e.g. waking, sleep, seizure). Crucial aspects of the signal may not be recognised by visual inspection of the EEG. The conventional method of sleep scoring is inadequate for quantitative EEG analysis because the definition of sleep stages is based on rather general and arbitrary criteria. Assessment of EEG variables by computer-aided methods of signal analysis, such as spectral analysis (decomposing a signal into its constituent frequency components) is an important method to investigate brain activity and provides complementary information to sleep stages. The fast Fourier transform (FFT) is a widely applied method for obtaining the EEG power density spectra. The spectrogram (i.e. colour-coded power spectra) of an entire nights' sleep provides a clear overview of the structure of a sleep recording even if sleep stages have not yet been visually scored.

An alternative approach to spectral analysis is analyzing signals in the time domain. Period-amplitude analysis (PAA) appears to be an attractive method because its concept is straightforward and easy to understand and it provides separate measures for the incidence and amplitude of waves. Problems arise, however, if PAA is applied to the raw EEG signal. The major problem is the dependency of measures in higher frequency bands on those in lower frequency bands. Particularly, incidence measures of higher frequencies are a mirror image of low frequency activity and thus may lead to misinterpretations. Therefore, PAA should be applied only to band-pass filtered signals.

For digital data processing, adequate low-pass filtering is necessary prior to sampling of the signals to avoid aliasing.

Notes

12 – Practical session

Standard procedures for adults in accredited sleep medicine centres in Europe

Jürgen Fischer, Zoran Dogas, Claudio L. Bassetti, Soren Berg, Ludger Grote, Poul Jennum, Patrick Lévy, Stefan Mihaicuta, Lino Nobili, Dieter Rieman, F. Javier Puertas Cuesta, Friedhart Raschke, Debra J. Skene, Neil Stanley, Dirk Pevernagie

Executive Committee (EC) of the Assembly of the National Sleep Societies (ANSS). Board of the European Sleep Research Society (ESRS), Regensburg, Germany

The presentation will describe standardised operational procedures (SOP) within clinical sleep medicine. As such, SOP procedures are a continuation of the previously published European guidelines for the accreditation of sleep medicine centres and European guidelines for the certification of professionals in sleep medicine, aimed at creating standards of practice in European sleep medicine. It is also part of a broader action plan of the European Sleep Research Society, including the process of accreditation of sleep medicine centres and certification of sleep medicine experts, as well as publishing the Catalogue of Knowledge and Skills for sleep medicine experts (physicians, non-medical health care providers, nurses and technologists), which will be a basis for the development of relevant educational curricula. In the current presentation, the SOP procedures for sleep medicine centres, regarding the diagnostic and therapeutic management of patients evaluated at sleep medicine centres, accredited according to the European Guidelines, are based primarily on prevailing evidence-based medicine principles. In addition, parts of the SOPs are based on a formalised consensus procedure applied by a group of Sleep Medicine Experts from the European National Sleep Societies. The final recommendations for standard operational procedures are categorised either as "standard practice", "procedure that could be useful", "procedure that is not useful" or "procedure with insufficient information available". SOPs described here include both subjective and objective testing, as well as recommendations for follow-up visits and for ensuring patients' safety in sleep medicine. The overall goal of the actual standard operational procedures is to further develop excellence in the practice and quality assurance of sleep medicine in Europe.

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Notes

13

Alterations of sleep-wake cycle in psychiatric disorders: an overview

Thomas Pollmächer

Center of Mental Health, Klinikum Ingolstadt, Ingolstadt, Germany

Insufficient sleep or reduced daytime alertness occur in the majority of psychiatric patients. Hence these are a non-specific but sensitive signs of mental disorders. For a substantial proportion of patients altered sleep wake behaviour is even the most prominent complaint.

Therefore, in any patients reporting insomnia or daytime sleepiness a detailed psychiatric work-up seems warranted. Primarily, this kind of work up targets symptoms of depression or anxiety and a detailed history regarding alcohol and drug intake is mandatory. The use of sleep diaries and actigraphy are particularly helpful in establishing a longitudinal view of the complaints. Polysomnographic recordings (PSG), which are not routinely performed, typically reveal less severe quantitative and qualitative disturbances of sleep as subjective complaints and sleep diaries suggest. However, PSG might reveal specific pathologies like PLMS or sleep apnoeas or hints for REM sleep abnormalities pointing to a depressive disorder. Daignostically, discrimination of daytime fatigue versus sleepiness is of particular importance in many subjects. Treatment of sleep-wake disturbances in psychiatric patients should primarily address the causative disease, for example major depression, panic disorder or (primary) insomnia. For primary insomnia, cognitive-behavioural approaches are highly effective and some elements of such programs, such as sleep restriction and stimulus control can be of great value also in other psychiatric disorders.

Notes

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Nosology and pathophysiology of insomnia

Dieter Riemann

Department of Psychiatry and Psychotherapy, Freiburg University Medical School, Freiburg, Germany

For the last two decades, several classification systems for insomnia have been suggested including DSM-IV, ICSD-1 and -2 as well as ICD-10 and research diagnostic criteria (RDC). All these systems have in common that for the diagnosis of insomnia apart from sleep related complaints daytime sequelae of the disorder have to be listed. In DSM-V instead of differentiating into primary and secondary insomnias a new category of “insomnia disorder” will be presented as the main category for insomnia. This main category will encompass several sleep-related complaints (prolonged sleep onset latency, increased number of awakenings, early morning awakening) as well as daytime related complaints like decreased attention and increased fatigue, heightened irritability or nervousness or frequent mood swings. According to DSM-V these symptoms will have to occur at least three times a week and have to persist for 3 months to be diagnosed as chronic insomnia. Instead of diagnosing insomnia as secondary, in the future the DSM-V system will allow to give comorbid diagnoses from the field of mental or somatic disorders.

Within the last decade concerning the pathophysiology of insomnia, especially the concept of a psychophysiological hyperarousal has gained wide-spread attention. Hyperarousal means increased activity either on a psychological or neurobiological level. Evidence comes from very different sources of research. On the one hand, it has clearly been shown that psychologically with respect to cognitive or emotional processes in insomniac patients, increased signs of hyperarousal, especially related to the process of sleep, are measurable. On the other hand, many studies from the field of neuroendocrinology or the autonomous nervous system have shown that the patients with insomnia, especially primary insomnia, do indeed display signs of hyperarousal. This for example applies to autonomous nervous system markers like heart rate or heart rate variability, or to psychoneuroendocrine variables like increased cortisol prior to or during sleep. With respect to electro- and neurophysiology it has been clearly shown that the sleep EEG of patients with insomnia is characterised by increased amounts in the fast frequency range and increased number of microarousals. Neuroimaging studies have confirmed that the brains of people with insomnia are less de-aroused than the brains of healthy sleepers during sleep. Insofar, the psychophysiological model of hyperarousal at present seems to be a most adequate model to characterize the pathophysiology of insomnia. Further details of the concept and implications for therapy will be encompassed in the presentation.

Notes

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Sleep features in insomniac patients

Mauro Manconi

Sleep and Epilepsy Center, Neurocenter of Southern Switzerland, Lugano, Switzerland

Abstract not received.

Notes

16

Mental and physical consequences of disturbed sleep

Thomas Pollmächer

Center of Mental Health, Klinikum Ingolstadt, Ingolstadt, Germany

Disturbed sleep may be a consequence of numerous mental and physical disorders and, in turn, disturbed sleep might compromise mental and physical health. Sleep disturbances considerably increase the risk for numerous psychiatric disorders, for depression in particular, although a causative relationship could not yet be firmly established. Ample experimental evidence suggests that sleep time reduction and decreased sleep continuity compromise metabolic networks and the immune system. Even short-term sleep disruption can impair glucose tolerance and specific immunity to viral antigens. In the clinical setting, some evidence suggests that chronic sleep disturbances going along with sleep disruption contribute to the risk for obesity and diabetes, whereas we do not know yet whether clinical sleep disorders negatively affect the immune system.

Notes

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Non-pharmacological treatment of insomnia

Dieter Riemann

Department of Psychiatry and Psychotherapy, Freiburg University Medical School, Freiburg, Germany

The non-pharmacological treatments of insomnia include mainly the cognitive behavioural treatment strategies for patients suffering from the disorder. These treatment strategies include relaxation techniques, psychoeducation (sleep hygiene), and specific cognitive behavioural treatments like stimulus control, sleep restriction and cognitive interventions to influence cognitive dysfunction in patients suffering from insomnia. These techniques may also be summarised as CBT-I. The last three decades have seen a plethora of well-designed and also randomized and controlled studies testing the efficacy of these treatment interventions for insomnia, especially primary insomnia. In summary, this research has clearly demonstrated that combined CBT-I programs are superior to any kind of placebo intervention or a waiting list control group. They are also equal in efficacy to short-term pharmacological intervention, like for example zolpidem. What is the interesting point is that the CBT-I techniques with regard to the long-term follow-ups, seem to have a more sustainable effect than pharmacotherapy. Usually it is the case with pharmacotherapy that patients fall back to their baseline levels of sleep functioning when discontinuing pharmacotherapy. This is not the case with CBT-I. What is a matter of discussion is the way CBT-I can be introduced into general care for patients with insomnia. No country up to now in the world has a system of CBT-I trained specialists, who treat patients afflicted with insomnia. Insofar, models of treatment delivery have to be devised. These include stepped care models, internet-based treatments or self-helped treatments. An overview of this discussion will be given in the presentation.

Notes

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The pharmacological treatment of insomnia

Thomas C. Wetter

Department of Psychiatry and Psychotherapy, University of Regensburg, Regensburg, Germany

There are various medications, substances, and preparations that may be used to treat insomnia. Physicians and patients should be aware of the indications, onsets of action, half-lives, and adverse effects, in order to ensure appropriate efficacy, decreased tolerance, and minimal safety-related issues. This is especially true when a patient with insomnia is considering use of a non-FDA-approved drug or substance for the condition. Benzodiazepines have been used to treat insomnia, but problems such as rebound insomnia, dependency, daytime drowsiness, and cognitive disturbances have resulted in prescribing this class of medications less frequently. Similarly, antidepressants with sedating properties such as trazodone, mirtazapine, and trimipramine are commonly prescribed to insomnia sufferers, despite considerable adverse effects such as orthostatic hypotension, blurred vision, and rarely priapism. Recently, doxepin in low dosage (1–6 mg) has been approved by the FDA for primary insomnia. Atypical antipsychotics such as olanzapine and quetiapine are also prescribed to patients with insomnia and also are associated with adverse effects that are not negligible, such as anticholinergic effects, and weight gain. Newer treatment options include medications acting on the alpha-1 subunit of the benzodiazepine receptor complex (Z-drugs) and a novel MT1/MT2 receptor agonist, ramelteon, have rapidly become the first-line therapy for patients with insomnia, in conjunction with behavioural therapy. Alternative therapies may appeal to those concerned about some of the negative side effects of traditional medical insomnia therapies. These treatments range from bright light therapy to herbal medications to biofeedback.

Notes

19 – Special lecture

Chronic insomnia and arousal – state of the science

Dieter Riemann

Department of Psychiatry and Psychotherapy, Freiburg University Medical School, Freiburg, Germany

Insomnia is one of the most frequent sleep disorders being more prevalent in women than in men and its prevalence increases with age. Insomnia is characterised by difficulties falling asleep, maintaining sleep, non-restorative sleep and associated daytime consequences like decreases in attention and concentration, heightened irritability and negative mood swings. It has also been shown, that chronic insomnia is coupled with an increased risk for depressive disorders in the long run. From a diagnostic point of view *primary insomnia* (PI) has to be differentiated from other types of insomnia related to other mental/somatic disorders or substance use/withdrawal. In DSM-V "Insomnia Disorder" will be introduced as a new general concept of insomnia. With respect to the diagnostic process, apart from clinical anamnesis, sleep questionnaires and sleep diaries play an important role to encompass all relevant symptoms. Current aetiological models of PI highlight the role of cognitive, emotional and physiological hyperarousal for the development and maintenance of the disorder. The so-called 3P model posits that there are important premorbid, precipitating and perpetuating factors of high relevance for the aetiology and maintenance of the disorder. This presentation aims at reviewing the evidence for hyperarousal in insomnia with an emphasis on neurobiological studies. Indicators of physiological hyperarousal include EEG-derived polysomnographic variables, autonomous and neuroendocrine variables as well as outcome parameters of neuroimaging studies. So far, there is evidence that patients with insomnia show signs of increased autonomous and central nervous system arousal, as demonstrated by increased heart rate during sleep, increased amounts of fast frequencies in the sleep EEG, increased number of microarousals (especially during REM sleep) and a lesser deactivation of several brain areas during insomniac sleep compared to good sleep. However, we have yet to learn: 1) whether physiological hyperarousal is a cause or consequence of insomnia; 2) what is the genetic basis of hyperarousal and what is the impact of early-life stressors and other life events; and 3) what is the neurobiological basis of hyperarousal and how can it be modified in the most efficient manner without causing severe adverse effects.

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Notes

20–21 – Practical session

Clinical diagnosis of insomnia

Thomas C. Wetter

Department of Psychiatry and Psychotherapy, University of Regensburg, Regensburg, Germany

Insomnia comprises a range of clinical manifestations and involves a multitude of physical and psychological factors. As defined by the *International Classification of Sleep Disorders* (ICSD-2), a diagnosis of insomnia is characterised by both the existence of nocturnal symptoms and a clinically significant impact during daytime. Nocturnal symptoms include difficulty initiating or maintaining sleep, early awakening, and non-restorative sleep. Daytime symptoms include distress about poor nocturnal sleep and impairment of cognitive functions or other aspects of overall well-being. Researchers have traditionally used quantitative criteria to diagnose insomnia, but these criteria have not been standardised. The ICD-10 includes quantitative criteria for the frequency and duration of total wake time and/or total sleep time have been proposed. However, these criteria have not been uniformly employed. The assessment of insomnia starts with an initial diagnostic interview and the clinician must obtain sufficient information from the patient (and/or the bed partner) to correctly diagnose the insomnia subtype and contributing factors. Following the interview, subjective self-report measures are often helpful to supplement this information. Objective measures, such as laboratory tests, actigraphy, and overnight polysomnography, may be used to rule out suspected comorbid medical conditions and/or other sleep disorders when clinically indicated. This presentation focuses on assessment tools and discusses assessment procedures in a clinical setting along with a discussion of the subcategories of insomnia and their differential diagnosis.

Notes

22 – Practical session: case studies

Cognitive-behavioural insomnia treatment

Dieter Riemann

Department of Psychiatry and Psychotherapy, Freiburg University Medical School, Freiburg, Germany

Insomnia is defined as complaints of prolonged sleep latency, impaired sleep maintenance, non-refreshing sleep quality and associated daytime sequelae like increased fatigue, impaired concentration, irritable mood, etc. Insomnia is a frequent health complaint in western industrialised countries and chronically afflicts 10% of the adult population. Therapeutically, “sleeping pills” constitute the main therapeutic avenue of general practitioners towards combatting insomnia. At present, the so-called BZRA (benzodiazepine receptor agonists) encompassing classical benzodiazepine hypnotics and “newer”, but pharmacologically similar substances (i.e. zolpidem, zopiclone) dominate the field of prescriptions. BZRA have been criticised on many grounds, with respect to problems like development of tolerance, abuse and dependency potential, increase of nocturnal falls, memory impairments etc.

Insofar it is not surprising, that nowadays many experts in the field support CBT-I (cognitive behavioural treatment for insomnia) as the first line treatment, especially for chronic insomnia. CBT-I encompasses sleep hygiene, relaxation methods, stimulus control, sleep restriction and cognitive techniques to reduce worrying and ruminations. The evidence base for CBT-I is very impressive now with 5 published meta-analyses indicating clear-cut benefits not only during active therapy but also at follow-ups. A major problem with CBT-I is dissemination to both health care professsionals and patients. Future strategies will include internet-based approaches to improve access to these methods. Recent additions to the canon of CBT-I include MCBT (mindfulness based cognitive therapy), ACT (acceptance and commitment therapy) and *Intensive sleep retraining*.

CBT-I methods not only are effective therapeutic tools but they can also be linked to psychoneurobiological models of chronic insomnia, i.e. the hyperarousal concept. A brief insight into ongoing research in this field linking the therapeutic arena with pathophysiology will be given.

Notes

23 – Practical session: case studies

Insomnia and hypersomnia as symptoms of mental disorders

Thomas Pollmächer

Center of Mental Health, Klinikum Ingolstadt, Ingolstadt, Germany

Subjective complaints of insomnia and hypersomnolence represent two sides of the same coin: disturbed sleep-wake regulation. The cases presented will help to understand how such complaints fit into the symptomatic pattern of mental disorders and what there importance is for diagnosis and treatment.

Notes

24 – Practical session: case studies

PSG evaluation of sleep in insomnia before and after treatment

Mauro Manconi

Sleep and Epilepsy Center, Neurocenter of Southern Switzerland, Lugano, Switzerland

Notes

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The obstructive sleep apnea syndrome

Winfried Randerath

Institute of Pneumology at the University Witten/Herdecke, Clinic for Pneumology and Allergology, Center of Sleep Medicine and Respiratory Care, Bethanien Hospital, Solingen, Germany

Due to its high prevalence of 2–14% of the population, the cardiovascular consequences, the risk of accidents, the impairment of quality of life and the socioeconomic burden, obstructive sleep apnea (OSAS) represents a major challenge for physicians and health care systems. Major risk factors for OSAS are obesity and skeletal malformations of mandible and face. These predisposing factors are associated with narrowing of the upper airways, leading to flow limitation and snoring. During sleep, the compensatory activity of the upper airway muscles fails, leading to reduction or cessation of airflow. There is evidence of structural changes of upper airway nerves and muscles, contributing to the obstruction. Recently, a fluid shift from the legs to the neck during the night has been discussed to contribute to the pathophysiology of sleep apnea. Apneas and hypopneas are associated with arousals from sleep disturbing sleep quality and leading to daytime symptoms such as cognitive impairment and daytime sleepiness. Moreover, they are associated with a continuous shift between oxygen desaturation and re-oxygenation which represent a major pathophysiological predisposition for cardiovascular consequences, such as arteriosclerosis. Thus, OSAS has a major impact on morbidity and mortality and should consequently be treated.

Notes

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Clinics and pathophysiology of CSA

Patrick Lévy[1,2]

[1]*Université Grenoble Alpes, HP2; Inserm, U1042, Grenoble, France*

[2]*CHU de Grenoble, Laboratoire EFCR, Pôle Locomotion Rééducation et Physiologie, Grenoble, France*

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Sleep apnea and cardiovascular diseases

Jean Louis Pépin[1,2], Renaud Tamisier[1,2], Patrick Lévy[1,2]

[1]*Université Grenoble Alpes, HP2; Inserm, U1042, Grenoble, France*

[2]*CHU de Grenoble, Laboratoire EFCR, Pôle Locomotion Rééducation et Physiologie, Grenoble, France*

The learning objectives will be the following:

1. Understand the mechanisms by which Intermittent hypoxia (IH) is inducing oxidative stress and consequently promotes inflammation, endothelial dysfunction and cardio-metabolic morbidity.
2. Understand the links between obstructive sleep apnea (OSA) and cardiovascular diseases, diabetes and non-alcoholic fatty liver diseases.
3. Discuss whether effective treatment of OSA may represent an important target for improving cardio-metabolic risk.
4. Understand that response to CPAP therapy in terms of cardiovascular and metabolic outcomes differs in non-obese and obese OSA patients.
5. Understand how the failure of CPAP to alter metabolic or inflammatory markers in obese OSA emphasizes the need to offer a combination of multiple modalities of treatment including weight loss and physical activity.

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Sleep disordered breathing and stroke

Claudio L. Bassetti

University Hospital, Bern, Switzerland

Frequency. Sleep disordered breathing (SDB) is present in over 50% of patients with acute stroke[1–3]. This frequency is higher in patients with haemorrhagic and/or severe stroke, lower in patients with chronic stroke and transient ischaemic attacks[1,4]. An association between SDB and specific subtypes of strokes (nighttime and wake up stroke, lacunar stroke, stroke associated with patent foramen ovale...) has been suggested in some studies[5].

Most commonly patients with stroke present a SDB of obstructive of mixed type. In the very acute phase of stroke, in patients with cardiac failure, and in patients with lesions in the central autonomic network central SDB of central type may dominate the picture[6,7].

Implications. A) patients with SDB have an increased independent risk of stroke, including silent stroke[8,9]. This maybe due to such factors as hypertension, diabetes, cardiac arrhythmias, hypoxia-related endothelial damage, and changes of cerebral haemodynamics[10,11]. B) In the acute phase of stroke, the presence of haemodynamic swings and recurrent hypoxias secondary to SDB, can lead to a reduction of cerebral perfusions/oxygenation and by this a more severe stroke extension[12,13]. C) In post-stroke patients, SDB increases the long-term risk of recurrence, poor functional outcome, and mortality[3,14,15].

Treatment of SDB decreases the risk of stroke and the risk of recurrences after stroke[16]. Some studies suggest also a positive effect of SDB treatment (CPAP) on neurological outcome after stroke[17–19]. First studies found a low CPAP compliance in stroke patients with SDB[2,3,20]. In the very last few years, however, several studies have proven that even in this difficult clinical setting CPAP treatment is feasible (acceptable compliance) and cost-effective[17,18,21,22].

SAS-CARE is an ongoing multi-centre study which assesses the effect of SDB (and CPAP treatment) on short- and long-term outcome of stroke[23,24].

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Sleep apnea and cognitive alterations

Luigi Ferini-Strambi

Sleep disorders Center, Dept. of Neuroscience, Università Vita-Salute San Raffaele, Milan, Italy

Obstructive sleep apnea (OSA) has been associated with a broad range of neurocognitive difficulties. The current view is that the neurocognitive impairment in OSA is due to the adverse effects of sleep fragmentation and/or intermittent hypoxia. The overall picture of cognitive deficits in OSA is complex. The negative effects of OSA on cognition have been evaluated into four discrete domains: intellectual function, memory, attention, and executive function. High intellectual function may protect against the deterioration of some cognitive abilities in some OSA patients. Recent papers suggest that OSA may impair only some aspects of memory: patients perform significantly worse on tests of verbal memory, but not visual memory, when compared with controls. The ability to maintain alertness over time is important in order to perform adequately during wakefulness. Differences between individual with OSA and controls have been shown on traditional neuropsychological tests of attention[1]. Executive functions collectively manage higher order cognitive processes, and are responsible for volition, planning, purposeful action and monitoring effective performance. Some studies have shown that executive function may be significantly impacted by OSA: specifically, patients show impairment on tests that require set shifting, mental flexibility, and planning[2,3].

Continuous positive airway pressure (CPAP) is the most effective and widely used treatment of OSA. In the majority of studies of OSA patients treated with CPAP, attention/vigilance improved, but changes in global functioning, executive functioning, and memory improved in about half of the studies. This may be due, in part, to variability in study design and sampling methodology across studies[4].

Structural volume changes have been demonstrated in brain regions of OSA patients including areas that regulate memory and executive function (e.g., frontal cortex, anterior cingulate, and hippocampus). Growing evidence suggest the OSA-related changes in brain morphology may improve with CPAP treatment[5]. Neuroimaging studies performed during cognitive testing have provided insight into CPAP's effect on function of neuroanatomical circuits in the brain. Although neuroimaging can provide important insights into the structural and functional differences associated with OSA, one of the challenges is to interpret the findings in light of comorbid conditions that also cause neural injury.

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Different approaches to sleep apnea treatment

Winfried Randerath

Institute of Pneumology at the University Witten/Herdecke, Clinic for Pneumology and Allergology, Center of Sleep Medicine and Respiratory Care, Bethanien Hospital, Solingen, Germany

Obstructive (OSAS) and central sleep apnea (CSA) should be differentiated as precisely as possible because of different therapeutic consequences. OSAS is characterised by an obstruction of the upper airways due to an imbalance between intraluminal pressure in the airways and extraluminal pressure (tissue). Continuous positive airway pressure (CPAP) is applied via a mask and increases the intraluminal pressure of the upper airway throughout the breathing cycle. It therefore counterbalances the narrowing of the upper airways. Mandibular advancement devices can be used in patients with mild to moderate sleep apnea (AHI < 25–30/h), while not severely obese (BMI < 30kg/m^2). In these cases the protrusion of the mandible enlarges the diameter of the upper airways. New therapeutical approaches include electrical stimulation of the hypoglossus nerve which stimulates the dilating muscles. The evidence for most other surgical or conservative options is very limited.

In central sleep apnea the stimulation of respiration is insufficiently generated in the brain stem. CPAP and application of oxygen resolve the central apneas in not more than 50%. However, the disturbances can be overcome in most cases by adaptive servo-ventilation. Therefore, the therapeutical algorithm starts with a short term CPAP trial, which is replaced by ASV if it fails.

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31 – Special lecture

Sleep apnea as a model of systemic disease

Patrick Lévy[1,2]

[1]*Université Grenoble Alpes, HP2; Inserm, U1042, Grenoble, France*

[2]*CHU de Grenoble, Laboratoire EFCR, Pôle Locomotion Rééducation et Physiologie, Grenoble, France*

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32 – Practical session

Diagnostic methods in sleep research

Thomas Penzel

Sleep Medicine Center, Charité Universitätsmedizin Berlin, Berlin, Germany

Diagnostic methods in sleep research start with a careful clinical interview supported by validated questionnaires. For sleep disordered breathing the most widely used questionnaires are the Berlin questionnaire and the STOP-BANG questionnaire, both with limitations.

Therefore the next step in the diagnosis of sleep disorders and in particular sleep disordered breathing is portable monitoring of respiratory functions (airflow, respiratory effort, oxygen saturation) cardiac function (heart rate or pulse rate or ECG), and some sleep functions (body position, movement patterns). Portable monitoring for sleep disordered breathing is the first diagnostic method not only in Germany but in many other countries as well. The conditions under which portable monitoring can be done with reliable results are now well defined. The limitations for the use of portable monitoring are specified as well. The devices used for portable monitoring are classified in four categories according to the number and the type of signals recorded.

The reference method for diagnosis is the attended cardiorespiratory polysomnography. An attended sleep study is also needed whenever new devices or systems need to be validated against the reference. Cardiorespiratory polysomnography records brain functions and sleep stages, respiratory, cardiac, and movement functions during sleep. The main advantage is that all changes can be related to the different sleep stages, to non-REM and REM sleep in particular. Arousal and sleep fragmentation can be quantified and evaluated in relation to changes in respiratory, motor and autonomic functions.

New technical developments use indirect assessment of sleep disordered breathing based on signals not directly recording respiration. The recording of ECG and deriving respiration, the analysis of the plethysmographically recorded pulse wave, the recording of jaw movements using magnets, and advanced analysis of respiratory sounds are recent approaches. These new methods are presented with few studies until now. Much research is currently ongoing here in order to make these less intrusive methods more reliable and in order to provide tools for a reliable and rapid assessment of sleep disordered breathing.

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33 – Practical session: case studies

Respiratory scoring

Jean Louis Pépin[1,2]

[1]*Université Grenoble Alpes, HP2; Inserm, U1042, Grenoble, France*

[2]*CHU de Grenoble, Laboratoire EFCR, Pôle Locomotion Rééducation et Physiologie, Grenoble, France*

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34 – Practical session: case studies

PAP treatment of sleep apnea

Jean Louis Pépin[1,2]

[1]*Université Grenoble Alpes, HP2; Inserm, U1042, Grenoble, France*

[2]*CHU de Grenoble, Laboratoire EFCR, Pôle Locomotion Rééducation et Physiologie, Grenoble, France*

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35 – Practical session: case studies

PAP treatment of sleep apnea

Patrick Lévy[1,2]

[1]*Université Grenoble Alpes, HP2; Inserm, U1042, Grenoble, France*

[2]*CHU de Grenoble, Laboratoire EFCR, Pôle Locomotion Rééducation et Physiologie, Grenoble, France*

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36 – Practical session: case studies

Sleep scoring

Birgit Högl

Department of Neurology, Innsbruck Medical University, Innsbruck, Austria

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Narcolepsy

Claudio L. Bassetti

University Hospital, Bern, Switzerland

Introduction. Narcolepsy was first reported by Westphal in 1877 and affects one out of 2000 adults in the general population[1].

Clinical manifestations. The leading symptom is an excessive, overwhelming daytime sleepiness, which is present in all patients [2]. The only pathognomonic symptom is cataplexy (sudden, short-lasting loss of muscle tone triggered by sudden emotions), which is present however only in 70–90% of patients and must be differentiated from physiological cataplexy-like disturbances[3]. About 50% of patients also present sleep paralysis and hallucinations at sleep onset or on awakening. Other sleep disturbances such as insomnia, restless legs syndrome, periodic limb movements in sleep, sleep disordered breathing, REM sleep behaviour disorder, and other parasomnias are not uncommon. additional manifestations of narcolepsy include mood changes, cognitive deficits, obesity/eating disturbances, endocrine changes, and pain[4].

Aetiology. Animal and human studies have shown that narcolepsy is usually linked to a reduction of hypocretin (orexin) neurons in the lateral hypothalamus, which results from the interaction between genetic predispositions (including HLA DQB1*0602) and non specific (infectious?) environmental factors[5–7]. The immune system is implicated in a molecular cascade of events eventually leading to the hypocretin deficiency[8].

Pathophysiology. Neurochemically narcolepsy is linked to multiple signalling deficits including the hypocretinergic and histaminergic systems[9]. Neurophysiologically it is best explained by a dyscontrol of state boundaries, the consequence of which are a desinhibition of REM sleep mechanisms and the occurrence of dissociated states. Recent studies have expanded our knowledge of narcolepsy as a brain disorder arising from the dysfunction of multiple brain areas including the hypothalamus, the amygdala, the medial prefrontal cortex, and the dorsal mesencephalo-pontine junction[10–12].

Diagnosis. The diagnosis of narcolepsy is made on clinical grounds. Neurophysiological tests (MSLT, polysomnography), HLA-typing and the assessment of hypocretin-1 levels in the cerebrospinal fluid can be used to confirm the diagnosis[13]. Sporadic idiopathic narcolepsy is most commonly observed. Rarely familial narcolepsy or narcolepsy-like syndromes secondary to brain disorders are found. In the absence of cataplexy the differential diagnosis includes sleep related breathing disturbances, chronic sleep deprivation, mood disorders, and other neurogenic hypersomnias.

Treatment. Management of narcolepsy is symptomatic but nevertheless often satisfactory[14]. Non pharmacological and pharmacological interventions are needed in most cases. Excessive daytime sleepiness is improved by drugs influencing the dopaminergic, and cataplexy by those modulating the noradrenergic transmission. Sodium oxybate is effective in improving both wake and sleep disturbances of narcolepsy. The role of immunoglobulins remains controversial[15].

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Idiopathic hypersomnia

Leja Dolenc-Grošelj

Institute of Clinical Neurophysiology, University Medical Center Ljubljana, Ljubljana, Slovenia

Idiopathic hypersomnia is a rare sleep disorder characterised by excessive daytime sleepiness with long and unrefreshing naps, prolonged and undisturbed nocturnal sleep, and great difficulty waking up (sleep drunkenness) after sleep. Reports suggest that patients with idiopathic hypersomnia represent only about 1% of patients seen in neurologic sleep centres and are 5–10-times less common than patients with narcolepsy. The disorder is familial in 50–60% of cases, most commonly in the classic form. HLA typing currently does not play a role in the diagnosis, and cerebrospinal fluid levels of hypocretin-1 are normal. The pathophysiology of idiopathic hypersomnia is unknown. The age at onset of symptoms varies, but it is commonly between 10 and 30 years. Nocturnal sleep is often long and undisturbed, with more than 10 hours of sleep. The *International Classification of Sleep Disorders* (ICSD) also recognises a second form of idiopathic hypersomnia without long sleep time. Polysomnographic findings include a short sleep latency, a high sleep efficiency (usually more than 90%), and increased amounts of deep (slow-wave) non-REM sleep. Findings on the *Multiple Sleep Latency Test* (MSLT) are the mean sleep latency less than 8 min and one or no sleep-onset rapid eye movement (REM) period (SOREMP). The patient's hypersomnia is not better explained by another sleep disorder, by a medical, neurologic, or mental disorder, or by medication use or substance abuse. The overall psychosocial handicap of patients with idiopathic hypersomnia is similar to that of patients with narcolepsy. Thus, idiopathic hypersomnia is a diagnosis of exclusion, and a broad differential diagnosis including narcolepsy with or without cataplexy, sleep-disordered breathing syndromes, behaviourally induced insufficient sleep syndrome, long sleepers, hypersomnia associated with psychiatric disorders should always be considered. Modafinil is considered to be the first-line treatment. In idiopathic hypersomnia, symptoms are generally stable and long lasting; spontaneous improvement in excessive daytime sleepiness may be observed.

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Hypersomnia and neurological disorders

Johannes Mathis

Sleep-Wake-Centre, Department of Neurology, University Hospital Inselspital, Bern, Switzerland

EDS and or hypersomnia in neurological patients is not only a consequence of the disease, but also due to drug treatment and co-morbid conditions, such as nocturnal pain, insomnia, nocturia, sleep apnoea syndrome, restless legs and periodic leg movements and – quite often – due to depression.

Hypersomnia is observed in up to 30% of stroke patients, most commonly in large bilateral thalamic or mesencephalic, large or multifocal cortical lesions. Prolonged sleep need is more often observed than increased sleep pressure, sometimes resulting in a peculiar "pre-sleep-behaviour".

After traumatic brain injury (TBI) hypersomnia is reported by 30% of patients, particularly with frontobasal, thalamo-diencephalic and hypothalamic lesions. Hypocretin loss in the early post-traumatic period has been reported, but a permanent loss of hypocretin was not confirmed.

Hypersomnia and EDS is a typical feature in viral or bacterial cerebral infections and paraneoplastic encephalopathy, whereas in multiple sclerosis, fatigue is often the most disabling symptom.

Frequency of hypersomnia in Parkinson's disease (PD) ranges up to 50%, particularly in more advanced disease and higher dopamine dosages. The clinical presentation varies from hypersomnia, permanent EDS to the rare sleep attacks with or without prior awareness and a narcolepsy type of EDS.

In dementia, sleep-wake rhythm disorders including sundowning syndrome, fragmented sleep and hypersomnia usually appear at an early stage. EDS is associated with greater functional impairment independently from cognitive impairment.

Neuromuscular disease is associated with sleep related breathing disorders in up to 40%, particularly after involvement of the phrenic nerve or diaphragm muscle or in the presence of obesity, restrictive lung disease or thoracic and cranio-facial malformations. Severe, narcolepsy type of hypersomnia or EDS was observed in myotonic dystrophy and considered to be of central, eventually hypocretinergic origin.

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REM sleep behaviour disorder

Luigi Ferini-Strambi

Sleep disorders Center, Dept. of Neuroscience, Università Vita-Salute San Raffaele, Milan, Italy

REM sleep behaviour disorder (RBD) is a multifaceted parasomnia involving REM sleep and the motor system in which there is a problematic behavioural release that is usually experienced by patients as enactment of distinctly altered, unpleasant, and combative dreams[1]. The vigorous and violent "oneiric" behaviours of RBD commonly result in injury, which at times can be severe and even life-threatening.

RBD is frequently interlinked with other sleep disorders, a wide range of neurologic disorders, and the pharmacotherapy of psychiatric and medical disorders, including antidepressants and beta-blockers. Experimental brainstem models of RBD in cats and rats, and a recently developed transgenic RBD mouse model with impaired GABA and glycine transmission[2], have expanded knowledge on brain mechanisms subserving REM-atonia and REM sleep phasic motor activity and their dysfunction in RBD[3].

Idiopathic RBD (iRBD) refers to RBD occurring in absence of any other obvious associated neurologic disorder. 'Secondary' or 'symptomatic' RBD refers to the combination of RBD plus another neurological disorder, such as neurodegenerative disease.

Moreover, an increasing amount of evidence shows that iRBD may be associated with several abnormalities, including an impaired cortical activity, neuropsychological deficits, brain MRI changes, olfactory and autonomic abnormalities. A better nosologic definition of the disorder is currently emerging from these studies. Taken together, these observations support the notion of RBD as an early manifestation of a more pervasive neurodegenerative process and challenge the concept of iRBD[4].

Longitudinal studies estimate that > 50% of patients with iRBD will develop neurodegenerative parkinsonism (almost exclusively Parkinson's disease, [PD], multiple system atrophy or dementia with Lewy bodies [DLB]). A very recent study showed that the rates of neurological-disease-free survival from time of iRBD diagnosis were 65.2% (95% CI 50.9 to 79.5) at 5 years, 26.6% (12.7 to 40.5) at 10 years, and 7.5% (–1.9 to 16.9) at 14 years[5]. Patients who remained disease-free at follow-up showed markers of increased short-term risk for developing PD and DLB in iRBD, such as decreased striatal DAT binding. These findings indicate that iRBD is a candidate for the study of early events and progression of the prodromal phase of neurodegenerative diseases, and to test disease-modifying strategies to slow or stop the neurodegenerative process.

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Sleep and epilepsy

Lino Nobili

Centre for Epilepsy Surgery "C. Munari", Centre of Sleep Medicine, Niguarda Hospital, Milan, Italy

The relationship between sleep and epilepsy has been known since Hippocrates who described nocturnal paroxysmal episodes characterised by fear, anger and wandering. With the development of the electroencephalogram (EEG) and successively with the application of Video-EEG techniques an accurate delineation of the reciprocal interactions between sleep and epilepsy has been provided. Sleep recording is now considered an important instrument for the diagnosis of patients affected by epilepsy; indeed sleep can facilitate the occurrence of interictal epileptic spikes, revealing alterations that are not visible during wakefulness and may help in the lateralization and localization of the epileptogenic zone. Video-polysomnography becomes mandatory when evaluating epileptic patients with sleep related seizures and can be useful for the differential diagnosis with other paroxysmal non-epileptic events and for the evaluation of possible comorbidities between sleep disorder and epilepsy.

There are specific epilepsy syndromes showing a strong association with sleep; the most important amongst these are nocturnal frontal lobe epilepsy, benign epilepsy with centro-temporal spikes, childhood epilepsy with occipital paroxysms, electrical *status epilepticus* during slow wave sleep and Landau-Kleffner syndrome. *Grand mal* seizures on awakening and juvenile myoclonic epilepsy occur on awakening from sleep in the early morning. Recently it has been shown that the presence of a Taylor's focal cortical dysplasia increases the risk of sleep-related seizures.

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Restless leg syndrome

Mauro Manconi

Sleep and Epilepsy Center, Neurocenter of Southern Switzerland, Lugano, Switzerland

Abstract not received.

Notes

43 – Special lecture

Sleep from the deep: what do intracerebral recordings tell us about sleep?

Lino Nobili

Centre for Epilepsy Surgery "C. Munari", Centre of Sleep Medicine, Niguarda Hospital, Milan, Italy

Human sleep is considered a global phenomenon, orchestrated by central specialised neuronal networks modulating the whole-brain activity. However, recent studies point to a local regulation of sleep. Sleep disorders, such as sleepwalking, suggest that electroencephalographic features of sleep and wakefulness might be simultaneously present in different cerebral regions. Recently, intracranial EEG recording techniques, mainly applied for the presurgical evaluation of drug-resistant epileptic patients, have provided new and interesting information on the activity of different cortical and subcortical structures during sleep in humans. In particular, it has been observed that the thalamus, during the transition between wake and sleep undergoes a deactivation process that precedes the one occurring within the cortex, with extensive cortical territories maintaining an activated pattern for several minutes after the thalamic deactivation. By performing simultaneous intracerebral electroencephalographic recordings from hippocampal as well as from distributed neocortical sites in neurosurgical patients, we observed that sleep spindles consistently occur in the hippocampus several minutes before sleep onset. Moreover, recent intracerebral EEG studies have also shown that human non-REM sleep can be characterised by the coexistence of wake-like and sleep-like EEG patterns in different cortical areas. In accordance, unit-firing recordings in multiple brain regions of neurosurgical patients evidenced that most sleep slow waves and the underlying active and inactive neuronal states do occur locally. These observations support the concept that wakefulness and sleep are not mutually exclusive states, but rather part of a continuum resulting from the complex interaction between diffuse neuromodulatory systems and intrinsic properties of the different thalamocortical modules. This interaction may account for the occurrence of dissociated activity across different brain structures characterizing both physiological and pathological conditions.

Notes

44 – Practical session

The assessment of EDS: different approaches

Leja Dolenc-Grošelj

Institute of Clinical Neurophysiology, University Medical Center Ljubljana, Ljubljana, Slovenia

Excessive daytime sleepiness (EDS) is a problem reported by 10–25% of the population, depending on the definition of sleepiness used and the population sampled. It is more frequent in young adults and elderly people. Sleepiness might be caused by reduced sleep time as often seen in otherwise healthy adults, by fragmented and disrupted sleep as found in patients with primary sleep disorders, by administration of sedating drugs and discontinuation of alerting drugs, and by various neurological disorders or primary sleep disorders (narcolepsy, idiopathic hyperomnia, etc). Sleepiness has a normal circadian rhythm that is increased in circadian rhythm misalignments such as those occurring in shift work or jet lag. The behavioural signs of sleepiness include yawning, ptosis, reduced activity, lapses in attention, and head nodding. Validated self-rated scales and physiological measures are available to assess the presence and degree of sleepiness. Among the various subjective measures of sleepiness, the Stanford Sleepiness Scale (SSS) is the best validated. It queire the individuals about how they feel at the present moment. Another perspective is to view sleepiness behaviourally, as in the likelihood of falling asleep, and thus ask individuals to rate that likelihood in different social circumstances and over longer periods. Epworth Sleepiness Scale (ESS) asks about falling asleep in settings in which patients typically report falling asleep (e.g., while driving, at church, in social conversation). The ESS has been validated in clinical populations showing a 74% sensitivity and 50% specificity relative to the *Mean Sleep latency Test* (MSLT) in a study of sleep disorders patients. The standard physiological measure of sleepiness, the MSLT, similarly conceptualizes sleepiness as the tendency to fall asleep by measuring the speed of falling asleep. The MSLT has gained wide acceptance as the standard method of quantifying sleepiness. Using standard polysomnographic techniques, the test measures, on repeated opportunities at 2-hour intervals throughout the day, the latency to fall asleep while lying in a quiet, dark bedroom. The metric typically used to express sleepiness has been average daily sleep latency (i.e., mean of the four or five tests conducted). In contrast to tests of performance, motivation does not seem to reduce the impact of sleep loss as measured by the MSLT. An alternative to the MSLT, is the *Maintenance of Wakefulness Test* (MWT). This test requires that subjects lie in bed or sit in a chair in a darkened room and try to remain awake. Like the MSLT, the measure of ability to remain awake is the latency to sleep onset. The test has not been standardised: there are 20-minute and 40-minute versions, and the subject is variously sitting upright in a chair, lying in bed, or semirecumbent in bed. The rationale for the MWT is that clinically the critical issue for patients is how long wakefulness can be maintained. The MSLT, on the other hand, addresses the question of the individual's risk of falling asleep by establishing a setting to maximize the likelihood of sleep onset. Thus, the MSLT identifies sleep tendency or clinically identifies maximum risk for the patient.

Excessive and persistent sleepiness is life-threatening, but when its presence is recognised objective documentation of sleepiness and its severity should be done. The aetiology of EDS should be identified, as it can be successfully treated or at least minimised.

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Notes

45 – Practical session: case studies

Excessive sleepiness

Luigi Ferini-Strambi

Sleep disorders Center, Dept. of Neuroscience, Università Vita-Salute San Raffaele, Milan, Italy

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46 – Practical session: case studies

Excessive sleepiness

Johannes Mathis

Sleep-Wake-Centre, Department of Neurology, University Hospital Inselspital, Bern, Switzerland

Notes

47 – Practical session: case studies

Movement disorders during sleep

Birgit Högl

Department of Neurology, Innsbruck Medical University, Innsbruck, Austria

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48 – Practical session: video cases

Epileptic paroxysmal events

Lino Nobili

Centre for Epilepsy Surgery "C. Munari", Centre of Sleep Medicine, Niguarda Hospital, Milan, Italy

This session will be focused on the semeiological features and the anatomo-electro-clinical correlations of sleep-related epileptic manifestations.

Frontal and extra-frontal sleep related seizures, characterised by different motor behaviours of increasing complexity and duration (brief automatisms, asymmetric dystonic or tonic posturing, hyperkinetic and violent behaviours, nocturnal wanderings), will be shown.

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Age-related sleep features in children

Oliviero Bruni

Centre for Pediatric Sleep Disorders, Department of Social and Developmental Psychology – Sapienza University, Rome, Italy

Childhood is characterised by larger amounts of SWS and REM sleep that decline during development and especially during adolescence. The maturation in sleep regulation processes is intense during the first months of life until the age of 4–5 years[1], and from the age of 5 to 6 years, the architecture of sleep becomes progressively closer to that of young adults and sleep stages (REM and non-REM) become well established.

The most important time-points in sleep development in children can be summarised as follows:

- 2–3 months: appearing of homeostatic mechanism of sleep, maturation of EEG patterns
- 3–5 years: disappearing of naps, non-REM redistribution during the night
- adolescence: synaptic pruning, theta and delta EEG power decline

In the 1st month of life the neonate shows a polyphasic S-W rhythm with cycles of 3–4 hours but between 1st and 4th month there is a progressive adaptation to light-dark cycle with sleep period distributed during the night. The first sign of circadian rhythm is the appearance (at 3–4 weeks) of a long phase of agitated wake with crying between 5 and 10 p.m., commonly recognised as hunger or abdominal pain (colic). At 6 months, the longer sleep period is about 6 hours and there are two sleep bouts interrupted by one awakening to eat.

The sleep EEG pattern changes rapidly during the first months through different steps:

- disappearance of *tracé alternant* between 1st and 2nd month;
- appearance of spindle between 6th and 9th week;
- K complex appears at about 5 months of age;
- differentiation of non-REM stages between 1½–3 months and distinction between non-REM stages 3 and 4 possible at 5th–6th month;
- sleep onset in REM stage before 2nd–3rd month.

Sleep changes in the period of age between 1st and 5th year:

- sleep onset latency averages 15–30 minutes;
- stage 2 non-REM appears within 3–4 minutes after the sleep onset, and 3–4 non-REM within 15 minutes;
- non-REM sleep mainly distributed during the first third of the night;
- the first REM period within 1 hour after sleep onset
- REM decrease from 30% to 20–25% (adult level);
- cycle lengths increase from 40 minutes at 2 years to 60 minutes at 5 years;
- 7–10 sleep cycles, with 3.5 stage shift for hour.

Sleep changes in the period between 6 and 12 years of age:

- sleep latency exceeds 15 minutes;
- first REM often missing;
- REM latency averages 140 minutes;
- SWS increases in the first part of the night;
- total sleep time declines with the increasing age, but still 2 hours more than adult;
- progressive delay in sleep onset (20 at 5 years; 21 at 8 years ; 22 at 10 years);
- body movements decrease in frequency.

Sleep changes during adolescence:

- time spent in bed and total sleep time decrease, resulting in a cumulative sleep debt;
- delay in time of sleep onset (for social habits);
- sleep duration in prepubescent: 10 h; mid-adolescence: 8.5 h; adolescence: 7 h;

- increased daytime sleepiness;
- slow wave sleep decreased significantly associated with delta and theta EEG power decline;
- the REM and non-REM percentages reach adult levels.

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Sleep and cognitive function in children

Oliviero Bruni[1], Raffaele Ferri[2]

[1]*Centre for Pediatric Sleep Disorders, Department of Social and Developmental Psychology – Sapienza University, Rome, Italy*

[2]*Sleep Research Centre, Department of Neurology I.C., Oasi Institute (IRCCS), Troina, Italy*

The role of sleep for daytime functioning and neurocognitive performance in infants and children is mediated by the process of sleep-related neural plasticity[1]. A close relationship exists between the development of sleep features, brain maturation and various cognitive processes. Three specific oscillatory patterns of sleep (sleep spindles, cyclic alternating pattern [CAP] and Slow wave activity [SWA]) have been related to memory consolidation and cognitive abilities in adults and children and their age-dependent developmental trajectory may be associated with the evolution of plasticity and maturation processes[2].

System consolidation of memory might take place during slow-wave sleep (SWS) rather than during rapid eye movement (REM) sleep[1]. Memory consolidation during SWS is orchestrated by the neocortical < 1Hz electroencephalogram (EEG) slow oscillations and involves the reactivation of newly encoded representations and their subsequent redistribution from temporary hippocampal to neocortical long-term storage sites. This “cognitive” role of SWS is extremely important in childhood because non-REM sleep EEG synchronization changes considerably with age, and the highest levels of SWS and of slow wave activity (SWA) occur during childhood.

The other sleep EEG patterns that play an important role in the consolidation and reorganization of memories are sleep spindles that represent the markers of the thalamo-hippocampo-cortical network activation and provide the conditions for synaptic change associated with the offline consolidation of declarative and procedural memory[3].

CAP is the third EEG pattern correlated with cognitive performances: non-verbal fluid-reasoning ability was positively associated with EEG slow oscillations (A1 phases) during SWS[4].

Neurophysiological and neuroimaging analysis of the development of sleep-dependent plasticity markers (i.e. spindles, CAP, SWA) in children could allow to understand the pathophysiological conditions subtending the long-term disruption of cerebral plasticity processes involved in memory consolidation during sleep.

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Insomnia

Oliviero Bruni

Centre for Pediatric Sleep Disorders, Department of Social and Developmental Psychology – Sapienza University, Rome, Italy

Maturational processes are involved in the consolidation of sleep and in the adaptation of the sleep-wake rhythms of the infants to the 24 hours cycle. These processes take place during the first months of life and are based on the interactions of several factors such as neurophysiological development, individual characteristics of the child, environmental influences. In the majority of children this process evolves smoothly, without crisis or abrupt steps. However, in about 20–30% of children this process is longer, difficult and the child's own rhythm tends to persist fighting with the parents' attempts to regulate on appropriate schedule. The main manifestation of this unsuccessful adaptation is recurring night waking in a more or less cyclic manner. These awakenings are often associated with bedtime problems especially if the parental request of early bedtime crashes with the circadian typology of the child (if the child is an evening type, he/she tends to fall asleep later than normal, and the attempt to put him in bed at 7 or 8 p.m. will obviously lead to a fight).

Insomnia is one of the most common complaints in childhood and the prevalence varies with age: in the first two years is about 20–40% and from 3 years and remains constant at around 15%. The aetiopathogenetic basis is represented by the interactions of physiological, genetic and behavioural variables, in which parenting has an important role (incorrect behaviour at bedtime, feeding mode, co-sleeping, etc...). Only 20% of insomnia cases are based on organic causes in some diseases and the alteration of sleep is, at times, one of the most frequent symptom (gastroesophageal reflux, ear infections, allergies, etc...).

There is no clear consensus among sleep specialists as to the exact definition of childhood insomnia. The *International Classification of Sleep Disorders* (ICSD-2, 2005), defines the behavioural insomnia of childhood (BIC) as a difficulty in initiating and/or maintaining sleep whose aetiology is due to incorrect behaviour learned by the child.

The three subtypes of BIC, defined by the ICSD-2, are:

- BIC sleep-onset association type,
- BIC limit-setting type, and
- BIC combined type.

All three types include the primary difficulties of falling asleep independently or frequent night awakenings.

Our vision, however, is a little bit different, since – from the clinical perspective – we can identify a sort of genetic predisposition to insomnia presented with different "insomnia phenotypes":

- insomnia with no difficulties in falling asleep and mid-night awakenings,
- insomnia with difficulty in falling asleep (kicking legs) and nocturnal hyperactivity,
- insomnia with difficulty in falling asleep and multiple night awakenings.

These three different phenotypes have a different origin for the insomnia and require completely different treatments.

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Hypersomnia

Fabio Pizza[1,2]

[1]*Department of Biomedical and Neuromotor Sciences (DIBINEM), University of Bologna, Bologna, Italy*

[2]*IRCCS Institute of Neurological Sciences, AUSL Bologna, Bologna, Italy*

The term hypersomnia depicts a condition characterized by excessive daytime sleepiness, the subjective feeling of drowsiness during daytime leading to altered cognitive functioning, increased sleep need during the day and/or sleep episodes occurring in inappropriate (potentially dangerous) situations. Hypersomnia can be either a symptom of several sleep disorders (secondary hypersomnia), such as obstructive sleep apnea or circadian rhythm sleep disorders, or the cardinal manifestation of the hypersomnias of central origin (primary hypersomnias). Primary and secondary hypersomnias have different clinical features: patients with obstructive sleep apnea generally suffer from a constant drowsiness feeling during daytime, patients with idiopathic hypersomnia report an increased sleep need and "sleep drunkenness" in the morning, while patients with narcolepsy can experience the occurrence of abrupt sleep attacks and are generally refreshed by short sleep episodes (associated with dreaming related to REM sleep occurring at the sleep onset)[1].

Different tools have been developed to assess daytime somnolence: subjective "trait" sleepiness can be measured with scales, the most used being the Epworth sleepiness scale[2], whereas the objective sleep propensity or the ability to maintain wakefulness are quantified in the sleep laboratory by the *Multiple Sleep Latency Test* (MSLT) or the *Maintenance of Wakefulness Test* (MWT)[3]. While subjective sleep measures should be collected for both primary and secondary hypersomnias (both at diagnosis and at follow up after appropriate treatments), objective tests are administered in more specific conditions: the MSLT is a diagnostic test to classify the hypersomnias of central origin (not useful to quantify sleepiness in secondary hypersomnias) for its potential to assess sleep propensity and the occurrence of sleep onset REM periods, whereas the MWT is a non diagnostic tool to measure resistance to sleepiness useful to assess response to treatment in primary hypersomnias or to objectively measure the ability to maintain wakefulness in workers (e.g. professional drivers) who could be dangerous for themselves and the others.

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Non-REM parasomnias

Lino Nobili

Centre for Epilepsy Surgery "C. Munari", Centre of Sleep Medicine, Niguarda Hospital, Milan, Italy

Non-REM arousal parasomnias are generally benign sleep related paroxysmal behaviours with well established features. The hallmarks of arousal parasomnias are onset during non-REM slow wave sleep (although episodes arising from stage 2 non-REM sleep are documented) and a lack of conscious awareness or memory of the event; the event is characterised by the presence of automatic behaviours. The standard classification of sleep disorders classified arousal parasomnias into three distinct forms, depending on the amount of motor and autonomic involvement: confusional arousals, sleepwalking, and sleep terrors. However, this classification into strict distinct categories is probably an oversimplification; recent observations indicate the presence of a hierarchical continuum between the different behavioural patterns of arousal parasomnias.

A breakdown of boundaries between wakefulness and non-REM sleep, resulting in the co-existence of these two states, is considered to be the basis of arousal parasomnias. Routine scalp EEG during arousal parasomnias often shows the presence of high-amplitude slow waves with superimposed wake-like activity (α and β activity). This could be the result of coexistence of different local behaviours: local "awakenings" and local sleep. A SPECT study during sleepwalking found an increase in regional blood flow in the posterior cingulate cortex, while blood flow in the frontoparietal associative cortices was decreased. In line with this finding intracerebral EEG investigation showed the presence of local arousal of the motor and cingulate cortices associated with increased delta activity in the frontoparietal and associative cortices.

The differential diagnosis between non-REM parasomnias and sleep-related epilepsies may be difficult because of the possible clinical similarities between the two disorders, particularly when affective symptoms or ambulatory behaviours characterize the paroxysmal episodes. Several attempts have been made to define specific and reliable clinical diagnostic criteria and to describe peculiar semeiological patterns recognizable by Video-Polysomnographic recordings; however, the differential diagnosis still remains challenging in some cases, especially if epilepsy and parasomnia coexist in the same subject.

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Sleep apnea in paediatric patients

Reinhold Kerbl

Department of Pediatrics and Adolescent Medicine, General Hospital of Leoben, Leoben, Austria

Definition. Among several different definitions, an age-specific definition seems to be mostly appropriate. In infants, a respiratory arrest of ≥ 3 s may be classified as apnea. In older children, a duration of ≥ 5 s appears to be reasonable. Apneas may occur as single events or as periodic apneas. According to Kelly, periodic breathing is defined as at least three central apneas of at least 3 s duration, interrupted by breathing of ≤ 20 s. There is no overall consensus which duration of single apneas and which density of repeated apneas have to be considered as "pathological". In general, central apneas up to 12 s (15 s) are considered as normal in young children, in older children even 20 s may be accepted as "normal", especially if associated with a sigh. For obstructive apneas, usually cut-off values between 3 s and 5 s are applied. Altogether, the clinical impact of apneas, however, does not only depend on their duration, but also on concomitant features (gasping, desaturation, hypercapnia, bradycardia).

Types of apneas and age dependency. As in adults, apneas may be classified as central, obstructive or mixed. For reliable diagnosis, polygraphic investigations are needed. These have to consider age-specific properties of respiration frequency which may be as high as 60/min or even more in newborns. Typical age-dependent features are (central) apneas of prematurity and obstructive apneas in pre-school children due to adenotonsillar hyperplasia. Central apneas may also be associated with CNS anomalies (e.g. Arnold Chiari syndrome), while obstructive apneas (OSA) also occur in different malformation syndromes (e.g. Pierre Robin syndrome).

Treatment depends on the underlying type and cause of apnea. While apneas of prematurity may be treated with caffeine, OSA in pre-school and school children can be cured by adenotonsillectomy or adenotonsillotomy in most patients. Only in few cases CPAP or bi-level mechanical ventilation is needed. Specific syndromes associated with apneas require a specific "patient-tailored" approach. Treatment efficacy should be controlled by follow-up polygraphy whenever possible.

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55 – Special lecture

What makes paediatric sleep medicine different?

Reinhold Kerbl

Department of Pediatrics and Adolescent Medicine, General Hospital of Leoben, Leoben, Austria

Social background and age-specific sleep disorders. In contrast to sleep disorders in adults, sleep disorders of children "affect" the whole family. Parents and caregivers are concerned about the sleep problem of their infant or child, and parents themselves suffer from reduced sleep quantity and poor sleep quality. "My child cannot sleep" is frequently reported by parents to relatives and friends or via social media, but only few affected families find the way to professsional help.

One problem in infants is the still incompletely developed circadian rhythm, keeping parents awake during night. In pre-school children, problems with falling asleep are frequent, and in many cases are due to the lack of consequent parental behaviour. In school-age children, reduced sleep quantity and anxiety may become a problem. Finally, the "social jetlag" resulting from extremely delayed bedtimes is typical for adolescents.

Organic vs. non-organic sleep disorders. As in adults, the majority of sleep disorders are non-organic. For these cases, a careful history is essential to define the actual problem. Age-specific questionnaires and sleep protocols are helpful for this purpose. If the collected material is unsuspicious of an organic sleep problem, polysomnographic investigation is not indicated. However, if anamnesis and clinical findings point towards an organic reason, polysomnographic recordings should be performed in a sleep lab especially equipped for investigations in children.

Equipment and staff. Especially in infants and young children, mounting of electrodes and fixation of probes represent a challenge for nurses or technicians, and sometimes need much patience. For recording and analysis of EEG, sleep stages and different physiological parameters, the age-specific properties have to be considered, and paediatric somnologists must know about changes by age.

Treatment. In case of non-organic sleep disorders, a behavioural approach is successful in most cases, however has to include the whole family. Among organic sleep disorders, obstructive sleep apneas (OSA) are the most frequent finding, requiring ENT surgery. Altogether, paediatric somnologists have to cooperate with several other specialised professionals to design the most appropriate treatment in all cases.

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Notes

56 – Practical session

The assessment of sleep-wake disorders in children

Barbara Gnidovec-Stražišar

Department of Child, Adolescent and Developmental Neurology, Children's Hospital, University Medical Centre Ljubljana, Slovenia

Sleep-wake rhythm disorders are characterised by normal sleep quantity and quality at the wrong time as dictated by societal or familial demands. The circadian pacemaker may be delayed or advanced with respect to the desired hour of sleep, or clock time and circadian time may be out of phase. The estimated prevalence of circadian rhythm disorders in children is at least 10%[1].

As in any other sleep disorder in children, a detailed sleep history is essential to distinguish circadian rhythm disorders from other conditions. The hallmark is that when the child is permitted to sleep on his/her desired schedule, sleep is normal and daytime sleepiness rapidly subsides. Therefore it is very helpful to determine child's sleep-wake patterns over time. This information can be readily obtained by using sleep diaries and sleep logs. Graphic recording of bedtime, latency to sleep onset, night wakings, time of morning offset and frequency, timing and length of daytime naps are considerably more helpful in visualizing child's sleep-wake cycles and can provide useful information to support the clinical history and also provide baseline reference for later management. Two weeks of baseline sleep diaries is usually adequate to delineate sleep patterns[2]. Parents are usually those who fill in sleep diaries; however in older children and adolescents more accurate information may be obtained by having the patient complete the sleep log by himself. The information obtained by recording of child's sleep-wake behaviours over 24-hour period using sleep diary is however very subjective. Continuous activity monitoring by actigraphy enables more objective assessment of child's rest-activity patterns in the naturalistic home setting. A portable wristwatch-like device records and store information regarding body movement over a period of time and later off-line analysis using computer software conveys this information to approximate sleep-wake patterns. Sleep state monitoring by actigraphy has been shown to be consistent with PSG when assessing certain parameters of sleep and sleep-wake cycle in children[3]. Actigraphy however is most useful in delineating sleep patterns and in diagnosing circadian rhythm disorders[4]. It also more accurately documents sleep duration, night-wakings and less reliably sleep onset latency in patients in whom there appears to be discrepancy between subjective sleep complaint and daytime consequences.

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57 – Practical session

Sleep scoring in children

Oliviero Bruni

Centre for Pediatric Sleep Disorders, Department of Social and Developmental Psychology – Sapienza University, Rome, Italy

The most important determinant of sleep changes during development is the age. The *Pediatric Task Force of American Academy of Sleep Medicine* (AASM), as part of the Committee for the new sleep scoring manual, developed a comprehensive literature-based review of the changes of sleep structure during development in order to define the differences between adult and child sleep macrostructure[1]. They reported several differences, summarised as follows:

Wakefulness (W). The dominant posterior rhythm (DPR) of relaxed wakefulness increases in frequency with age:

- 3.5–4.5 Hz in 75% of normal infants by 3–4 months post-term;
- 5–6 Hz in most infants 5–6 months post-term;
- 6 Hz in 70% of normal children by 2 months of age; and
- 8 Hz (range 7.5–9.5 Hz) in 82% of normal children aged 3 years, 9 Hz in 65% of 9-year-olds, and 10 Hz in 65% of 15-year-old controls.

Stage 1 non-REM (N1). Non-REM sleep stage 1 in an infant or child can be scored if the dominant posterior rhythm occupies < 50% of a 30-second epoch, and one or more of the following EEG patterns appear:

- a diffuse lower voltage mixed frequency activity;
- hypnagogic hypersynchrony;
- rhythmic anterior theta of drowsiness;
- diffuse high voltage occipital delta slowing;
- runs or bursts of diffuse, frontal, frontocentral, or occipital maximal rhythmic 3–5 Hz slowing;
- vertex sharp waves; and/or
- post-arousal hypersynchrony.

Vertex sharp waves are best seen over the central (Cz, C3, C4) and K complexes over the frontal (Fz, F3, F4) electrodes.

Stage 2 non-REM (N2). Stage N2 is scored when the typical phasic EEG patterns of this stage (spindles and/or K complexes) are clearly recognizable.

Sleep spindles in children (typically present by 2 to 3 months post-term) occur independently at two different frequencies and two different scalp locations: 11.0–12.75 Hz over the frontal and 13.0–14.75 Hz over the centro-parietal electrodes; these findings are most prominent in children younger than 13 years. About 50% of sleep spindles within a particular infant's PSG are asynchronous before 6 months of age, 30% at 1 year. K complexes first appear 5 months post-term and are usually present by 6 months post-term.

Stage 3–4 non-REM (N3). Stage N3 is scored when > 20% of the 30-second epoch contain slow wave activity (SWA) that is 0.5 to 2 Hz > 75 μV (usually 100–400 μV) activity. SWA of slow wave sleep (SWS) is first seen as early as 2–3 months post-term and is usually present 4–4.5 months post-term. SWA of SWS in an infant or child often has a peak-to-peak amplitude of 100 to 400 μV.

Summarizing and simplifying the scoring guidelines we can affirm that epochs of non-REM sleep which contain no sleep spindles, K complexes, or SWA would be scored as N1; those which contain either K complexes or sleep spindles and <20% SWS as N2, and those in which >20% of the 30-second epoch contain 0.5 to 2 Hz >75 μV (usually 100–400 μV) activity as N3.

Reference

1. Grigg-Damberger M, Gozal D, Marcus CL, Quan SF, Rosen CL, Chervin RD, et al. The visual scoring of sleep and arousal in infants and children. J Clin Sleep Med 2007; 3, 201–40.

Notes

58 – Practical session: video cases

Narco-cataplexy in children

Fabio Pizza[1,2]

[1]*Department of Biomedical and Neuromotor Sciences (DIBINEM), University of Bologna, Bologna, Italy*
[2]*IRCCS Institute of Neurological Sciences, AUSL Bologna, Bologna, Italy*

Notes

59 – Practical session: case studies

Insomnia treatment

Oliviero Bruni

Centre for Pediatric Sleep Disorders, Department of Social and Developmental Psychology – Sapienza University, Rome, Italy

Notes

60 – Practical session: case studies

Circadian sleep disorders

Reinhold Kerbl

Department of Pediatrics and Adolescent Medicine, General Hospital of Leoben, Leoben, Austria

The circadian rhythm plays an important role in sleep regulation, equally for children, adolescents and adults. The natural pre-existent circadian rhythm of about 25 hours is set to 24 hours by social circumstances and external stimuli (especially light).

In children and adolescents, different age-dependent circadian sleep disorders do occur and may cause problems not only for the patients themselves, but also for their families.

In newborns and infants, the circadian rhythm is incompletely developed, partly due to immature melatonin secretion. In older children, disturbed circadian rhythm may be part of a syndrome and may go along with an imbalance of melatonin, growth hormone and cortisol secretion (e.g. Smith Magenis syndrome). In other children, circadian sleep disorders may be secondary to CNS impairment (e.g. brain tumors). Finally, circadian sleep disorders in adolescents (e.g. delayed sleep phase syndrome) may cause relevant school, employment and other social problems. For the latter, modern technical devices (internet, mobile phone etc.) and so-called social networks may play an important role.

In this practical session, some typical age-specific cases are presented and discussed.

Notes

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K.-G. Henriksson (*Linkøping, Sweden*): Muscle pain in neuromuscular disorders and primary fibromyalgia

1987 **2nd Yugoslav Symposium on Neurourology and Urodynamics**
J. K. Light (*Houston, Texas, U.S.A.*): Neurogenic bladder in patients with spinal cord injury

1988 **Symposium on Quantitative Electromyography**
E. Stålberg (*Uppsala, Sweden*): Electromyography – reflection of motor unit's physiology in health and disease

1989 **Symposium on Sensory Encephalography**
A. M. Halliday (*London, Great Britain*): The widening role of evoked potentials in clinical practice

1990 **Symposium on Assessment of the Upper Motor Neuron Functions**
A. M. Sherwood (*Houston, Texas, U.S.A.*): Brain motor control assessment

1991 **Symposium on Neurophysiological Monitoring**
V. Deletis (*New York, N.Y., U.S.A.*): Intraoperative monitoring of evoked potentials – current status and perspective

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E. Rumpl (*Klagenfurt, Austria*): Neurophysiological evaluation of severe head injury patients

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H. Ikeda (*London, Great Britain*): Mammalian retinal neurotransmitters – as seen through the eyes of a neurophysiologist

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and

The First Lecture of the Slovene Basal Ganglia Club:
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1995 **Symposium on Multiple Sclerosis**
W. I. McDonald (*London, Great Britain*): The clinical and pathological dynamics of multiple sclerosis

1996 **Symposium on Update in Neurogenetics**
L. P. Rowland (*New York, N.Y., U.S.A.*): Molecular genetics and clinical neurology

1997 **Symposium on Cognitive Neuroscience**
G. Barrett (*Farnborough, Great Britain*): Cognitive neurophysiology, a tool for studying the breakdown of mental processes

1998 **9th European Congress of Clinical Neurophysiology, Ljubljana**
J. Trontelj (*Ljubljana, Slovenia*): SFEMG – Sensitive optics in space and time

1999 **Symposium on Electrophysiology of Hearing**
A. Starr (*Irvine, California, U.S.A.*): Mysteries of the cochlea

2000 **Symposium on Movement Disorders, "The Alpine Basal Ganglia Club"**
A. J. Lees (*London, Great Britain*): The relevance of pleasure/reward dopamine circuits to Parkinson's disease

2001 **EC-IFCN Ljubljana 2001 Regional EMG Refresher Course**
E. Stålberg (*Uppsala, Sweden*): The role of conventional and advanced electromyography in clinical neurology

2002 **International Symposium on Clinical and Electrophysiologic Diagnostics of Epilepsy**
P. Chauvel (*Marseille, France*): High-resolution electroencephalography in clinical neurophysiology: applications to epilepsy and evoked potentials

2003 **Symposium on Intraoperative Neurophysiology**
V. E. Amassian (*New York, N.Y., U.S.A*): Essentials of neurophysiology of the motor system

2004 **Symposium on Sleep Research**
M. Billiard (*Montpellier, France*): Excessive daytime sleepiness: clinical impression versus final diagnosis

2005 **37th International Danube Symposium for Neurological Sciences and Continuing Education**
T. Prevec (*Ljubljana, Slovenia*): Sharp or kind stimulus to activate the sensory system?

2006 **International Symposium on Spinal Cord Motor Control "From Denervated Muscles to Neurocontrol of Locomotion"**
G. Vrbová (*London, Great Britain*): Some observations on the biology of the neuromuscular system and their possible usefulness for recovery of impaired function

2007 **XVIth International SFEMG and QEMG Course and IXth Quantitative EMG Conference**
J. Kimura (*Kyoto, Japan*): The use of late responses as a quantitative measure of nerve conduction and motor neuron excitability

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C. L. Bassetti (*Bern, Switzerland*): Sleep, sleep disorders and stroke

2013 **2nd Alpine Sleep Summer School – an Introductory Course in Sleep Medicine**
P. H. Luppi (*Lyon France, Switzerland*): State of the neuronal network responsible for paradoxical (REM) sleep in neurological disorders

INVITATION TO DR. JANEZ FAGANEL MEMORIAL LECTURE & SYMPOSIUM 2014

We are glad to announce our 2014 autumn symposium with which we will celebrate its 30th anniversary. To mark this, Professor Milan R. Dimitrijević, founder of our Institute and the Janez Faganel Memorial lecture series, will present the 30th Memorial Lecture titled *The human lumbar cord conduction and processing capabilities and the spinal brain*, a review of the evolution of ideas on the role of the spinal cord in motor control. The old concepts on how the spinal neuronal networks operate, recently underwent marked changes. The notion that the neurons mediating spinal reflexes do not function independently of supraspinal neurons which can switch them form one mode of operation to the other, has significant impact in understanding the clinical neurophysiology for human upper motor neuron control.

Both Dr Janez Faganel's and Milan Dimitrijević's life-long interest is/was the physiology and pathophysiology of the spinal cord. The result of their pioneering work (from 1960 on) is the concept of "spinal brain" in the lumbar cord, a neuronal network which responds to the afferent input with a variety of transitory configurations and corresponding motor behaviour. Moreover, processing capabilities of the "spinal brain" can be modified with external electrical stimulation control and cellular implants. It is therefore self-evident why the title of the symposium will be *The Role of Spinal Brain in Human Motor Control: Concepts and Evidences.* Information and knowledge regarding human motor control plays an important role, especially in clinical medicine. The 2014 autumn symposium will be attended by leading experts in the field who will present their most current findings.

For more information please visit the Symposium website at:

http://www.kclj.si/ikn/DEJA/FAGA/F14_OS/F14.htm

Cordially invited to join us in Ljubljana on 5 September 2014!

Janez Zidar
Chairman, Dr. Janez Faganel Memorial Lectures Scientific Committee

Milan R. Dimitrijević
Founder of the Memorial Lecture Series & Symposium 2014 Scientific Organiser