ESRS - EU “Marie Curie” Project
2007-2010

Training in Sleep Research and Sleep Medicine

Final Symposium

Kultur und Bildungszentrum des Bezirks Oberbayern
Kloster Seeon

July 2nd - July 6th, 2010

Program & Abstracts

Program

Friday, July 2nd

h 20.00: *Dinner*

Saturday, July 3rd

h 7.30-8.30: *Breakfast*

h 8.30-9.00: Registration

h 9.00-9.30: Opening *(Festsaal)*

Claudio Bassetti *(Lugano/Zurich)*, **Roberto Amici** *(Bologna)*, **Thomas Pollmächer** (*Ingolstadt*)

Welcome from **Ernst Brinckmann**
Administrative Authority - District of Upper Bavaria

h 9.00-10.45: **Workshop. *New approaches in sleep research*** *(Festsaal)*

Chair: **Peter Achermann** (*Zurich*), **Patrick Levy** (*Grenoble*)
Discussants: **Philippe Peigneux** (*Bruxelles*), **Tarja Porkka-Heiskanen** (*Helsinki*)

h 10.45-11.15: *Coffee break*

h 11.15-13.00: Oral session I. *Clinical research* *(Festsaal)*

Chairs: **Pierre Aloise Beitinger** *(Munich)*
Sarah Loughran *(Zurich)*
Co-Chair: **Claudio Bassetti** (*Lugano/ Zürich*)

1 Relationship between inflammatory markers and sleep efficiency in kidney transplanted patients
Maria Czira, *Institute of Behavioural Sciences, Semmelweis University, Budapest, Hungary*

2 REM sleep behavior disorder in narcolepsy
Aleksandra Wierzbicka, *Institute of Psychiatry and Neurolgy, Warsaw, Poland*

3 Autonomic dysfunction in patients with obstructive sleep apnea-hypopnea syndrome
Sinziana Lovin, *University of Medicine and Pharmacy, Iasi, Romania*

4 The Daytime Functioning and Sleep Attribution Scale (DFSAS): A new insomnia-specific measure to probe daytime impairment and poor sleep attributions
Simon Kyle, *Glasgow Sleep Centre, Sackler Institute of Psychobiology Research, INS Glasgow, Scotland*

5 Insomnia is a predictor of depression- A meta-analytic evaluation of longitudinal epidemiological studies
Chiara Baglioni, *Department of Psychiatry and Psychotherapy, University of Freiburg, Germany*

6 Current study on sleep quality assessment in Georgian general population
Maia Alkhidze, *Research-Practical Centre for Prevention and Control of Epilepsy, Tbilisi, Georgia*

7 Switching Attention to Insomnia- the Role of Objective Sleep Duration
Julio José.Fernández-Mendoza, *Sleep Research and Treatment Center, Penn State College of Medicine, Hershey, PA, USA*

8 Effect of weight loss on inflammatory markers in overweight patients with mild obstructive sleep apnoea
Johanna Sahlman, *Dept. of Otorhinolaryngology, Kuopio University Hospital, Kuopio, Finland*

h 13.00-14.30: *Lunch*

h 14.30-16.00: Blitz session I. *Basic research* (Festsaal)

Chairs: **Davide Martelli** *(Bologna)*
Elizaveta Rutskova *(Moscow)*
Co-Chair: **Peter Achermann** (*Zurich*)

1 Sleep-dependent consolidation of temporal order in episodic memories
Manuel Schabus, *Laboratory for Sleep and Consciousness Research, Division Physiological Psychology, University of Salzburg, Austria*

2 A short nap reverses leukocyte increase induced by an acute sleep restriction
Michal Dyzma, *Unit 222 Sleep Research Unit, University Libre de Bruxelles, Montigny-Le-Tilleul Belgium*

3 Role of the lateral paragigantocellular nucleus in the regulation of paradoxical sleep in the rat
Chrystelle Sirieix, *Faculté de Médecine RTH Laennec, CNRS UMR 5167, Physiopathologie des Réseaux neuronaux du cycle veille-sommeil, Lyon, France*

4 Influence of sleep depth in an afternoon nap on the capacity to learn new information
Daria Antonenko, *Institute of Neuroendocrinology, University of Lübeck, Germany*

5 A prospective descriptive analysis of head jerks during sleep
Viola Gschliesser, *Dept. of Neurology, Innsbruck Medical University, Innsbruck Medical University, Austria*

6 Frequency and topography specific EEG activation during NREM and REM sleep prior to dream recall
Sarah Chellappa, *Centre for Chronobiology, Basel, Switzerland*

7 Sleep promoting substances and stroke recovery
Aleksandra Hodor, *Dept. of Neurology, University Hospital Zurich, Switzerland*

8 Intracranial evidence for human hippocampus involvement in motor sequence learning
Irina Oana Constantinescu, *University of Geneva, Switzerland*

9 Evidence that neurons of the sublaterodorsal tegmental nucleus triggering paradoxical (REM) sleep are glutamatergic
Olivier Clement, *UMR5167 Physiopathologie des réseaux neuronaux du cycle veille sommeil Lyon, France*

10 Induction of hippocampal theta rhythm after amphetamine microinjection into the ventral tegmental area in the rat
Magda Kusmierczak, *Animal Physiology, University of Gdansk, Poland*

11 Sleep entails arterial hypertension in hypocretin-deficient narcoleptic mice
Stefano Bastianini, *Department of Human and General Physiology, University of Bologna, Italy*

12 Applicability of shift-work protocols in rats; effects on body weight gain, behavioural activity and instrumental learning
Cathalijn Leenaars, *Sleep and Cognition, Netherlands Institute for Neuroscience, Amsterdam, The Netherlands*

13 PERIOD3 polymorphism, subjective and physiological sleepiness during day and night driving on real roads
Johanna Schwarz, *Stress Research Institute, Stockholm University, Sweden*

14 Association between fingers and images enhances the consolidation of procedural memory in serial reaction time task
Amir Homayoun Javadi Arjomand, *Psychology Department, Institute of Cognitive Neuroscience (ICN), London, United Kingdom*

15 Cholinergic mediation of enhanced REM sleep in conditional CRH-overexpressing mice
Maria Letizia Curzi, *Max Planck Institute of Psychiatry, Munich, Germany*

16 Losing consciousness-falling asleep during a go-no-go task
Tristan Bekinschtein, *Cognition and Brain Sciences Unit, Medical Research Council, Cambridge United Kingdom*

17 Influence of passive changes of bed climate on sleep quality
Katharina Ettenhuber, *Psychiatry, Sleep Department, Bezirksklinikum Regensburg, Germany*

18 Theory of mind and executive functions in Attention Deficit Hyperactivity Disorder (ADHD)
Alison Mary, *UR2NF, Universitè Libre de Bruxelles, Belgium*

h 14.30-16.00: Blitz session II. *Clinical research* *(Fürstenzimmer)*

Chairs: **Wytske Hofstra** *(Zwolle)*
Kai Spiegelhalder *(Freiburg)*
Co-Chair: **Joan Santamaria** (*Barcelona*)

1 Hyperarousal in insomnia
Ellemarije Altena, *Department of Clinical Neurosciences, Cambridge University,United Kingdom*

2 Sensations and pain in restless legs syndrome
Elias Karroum, *Pathologies du sommeil, Hôpital Pitié-Salpêtrière, Paris,France*

3 Memory Consolidation of a New Task is inhibited in Ethiopian Psychiatric Patients
Lisa Genzel, *Max Planck Institute of Psychiatry,Munich, Germany*

4 The role of psychological beliefs about sleep and insomnia and insomnia-related behavior in subjective and objective sleep
Elena Rasskazova, *Clinical psychology, Mental Health Research Centre of RAMS, Moscow, Russia*

5 Glucose Tolerance in Patients with Narcolepsy
Pierre-Alois Beitinger, *Max-Planck-Institute of Psychiatry, Munich, Germany*

6 Restless legs syndrome in patients with arterial hypertension
Samson Khachatryan, *Center for Neurology and Sleep Medicine, Yerevan, Armenia*

7 Vigilance in commercial vehicle operators
Mahssa Karimi, *Sleep Disorders Center, Pulmonary Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden*

8 Patients with sleep breathing disorders have normal global cognitive function
Lyudmila Korostovtseva, *Almazov Federal Heart, Blood and Endocrinology Centre, St. Petersburg Russia*

9 Secondary hypogonadism induced by severe obstructive sleep apnea syndrome (OSAS) and results after two months CPAP treatment
Raluca Mihaela Bercea, *Clinic of Pulmonary Diseases, Iasi, Romania*

10 How important is disturbed sleep for the patient with Parkinsons disease
MaartjeLouter, *Centre for Sleep Medicine "Kempenhaege", Heeze, The Netherlands*

11 Multicenter study about agreement between cpap titration by polisomnography and predictive formula in sahs patient
Jesus Escriba, *Clinical Neurophysiology Dept., University Hospital Doctor Peset, Valencia, Spain*

12 Nocturnal Low Oxygen Saturation As A Main Factor Of Excessive Daytime Somnolence
Alejandro Andrés Herrera Aceituno, *Departamento de Neurología y Neurocirugía, Hospital Clínico University of Chile, Santiago, Chile*

13 Sleep-related problems of Parkinsons disease in Lithuania
Dalia Mataciuniene, *Sapiega Hospital, Vilnius, Lithuania*

14 Assessment of sleep-wake behaviour in disorders of consciousness
Sarah Loughran, *University of Zürich, Zurich, Switzerland*

15 Vigilance Impairment in Narcolepsy
MadlenBach, *Dept. of Neurology, Sleep and Wake Disorders Center, University Hospital Zurich, Switzerland*

16 Inter-hemispheric spectral coherence reduction in sleep spindle frequency activity in patients with cognitive decline associated with aMCI and AD
Nicholas-Tiberio Economou, *Dept. of Psychiatry, Sleep Res. Unit, University of Athens, Greece*

h 16.00-16.30: *Coffee break*

h 16.30-17.30: Keynote lecture I. *The neuronal network responsible for paradoxical (REM) sleep and its dysfunctions in REM behavior disorder and narcolepsy* *(Festsaal)*

Pierre Hervé Luppi (*Lyon*)
Introduced by: **Irene Tobler** (*Zurich*)

h 17.30-18.45: Career Development. *How to write a scientific grant* *(Festsaal)*

Chair: **Zoran Dogas** (Split), **Tarja Porkka-Heiskanen** (*Helsinki*)
Discussant: **Derk-Jan Dijk** (*Guildford*)

h 20.30: *Dinner*

Sunday, July 4th

h 7.30-8.30: *Breakfast*

h 8.30-9.45: Round table I. *Which future for sleep research and sleep medicine?* (Festsaal)

Chairs: **Claudio Bassetti** (*Zurich*), **Thomas Pollmächer** (*Ingolstadt*)
Discussants: **Irene Tobler** (*Zurich*), **Malcolm Von Schantz** *(Guildford)*

h 9.45-10.45: Keynote lecture II. *Local sleep phenomena and intracerebral EEG recordings* (Festsaal)

Lino Nobili (*Milan)*
Introduced by: **Claudio Bassetti** (*Lugano/ Zurich*)

h 10.45-11.15: *Coffee break*

h 11.15-13.00: Oral session II. *Basic research* (Festsaal)

Chairs: **Loris Ferrari** *(Milan)*
Julie Vienne Bürki *(Lausanne)*
Co-Chair: **Tarja Porkka Heiskanen** (*Helsinki*)

1 Genome-wide association study identifies new HLA Class II haplotypes strongly protective against narcolepsy
Hyun Hor, *Center for Integrative Genomics (CIG), University of Lausanne, Switzerland*

2 Cortical gene expression during Paradoxical sleep as revealed by cDNA microarray and qPCR
Leslie Renouard, *UMR5167 Physiopathologie des réseaux neuronaux du cycle veille sommeil, Lyon, France*

3 Visuomotor learning and sleep slow-wave activity in children, adolescents and adults
Maya Ringli, *University Children's Hospital, Zurich, Switzerland*

4 Functional polymorphisms of DAT and COMT modulate slow wave sleep rebound after sleep deprivation in healthy humans
Sebastian Holst, *University of Zurich, Switzerland*

5 Sleep-related derangements of central autonomic and baroreflex control of heart period in leptin-deficient obese mice
Chiara Berteotti, *Dept. of Human and General Physiology, University of Bologna, Italy*

6 Study of the role of metabotropic glutamate receptors mGlu5 and mGlu7 on sleep and wakefulness in the rat
Maria Cavas, *Facultad de Psicologia, University of Malaga, Spain*

7 Grouping of MEG gamma band activity by spindles
Amr Ayoub, *Neuroendocrinology, University of Lübeck, Germany*

8 Effect of total sleep deprivation on endothelial function and heart rate variability in shift workers and non-shift workers
Sophie Wehrens, *Faculty of Health and Medical Sciences, Human Chronobiology, University of Surrey, Guildford, United Kingdom*

h 13.00-14.30: *Lunch*

h 14.30-16.00: Blitz session III. *Basic research* (Festsaal)

Chairs: **Caroline Harand** *(Caen)*
Manuel Schabus *(Salzburg)*
Co-Chair: **Irene Tobler** *(Zurich)*

1 The influence of amitriptyline on visual perceptual learning in healthy subjects
Monique Goerke, *Sleep research & Clinical Chronobiology, Department of Physiology Charité – Universitätsmedizin, Berlin, St. Hedwig Hospital, Germany*

2 Spectral composition of daily light exposure in young adults in summer and winter
Helen Thorne, *Surrey Sleep Research Centre, Faculty of Health and Medical Sciences, Guildford United Kingdom*

3 Sleep and Environmental Context - Interactive Effects for Memory
Scott Cairney, *School of Psychological Sciences, University of Manchester, United Kingdom*

4 Interrelationship between baseline sleep architecture, circadian activity pattern and cognitive deterioration in the APP23 mouse model of Alzheimer's disease
Elly Geerts, *University of Antwerp, Wilrijk, Belgium*

5 The effects of trait and state activation on daytime sleepiness after partial sleep deprivation
Marija Bakotic, *Institute for Medical Research and Occupational Health, Zagreb, Croatia*

6 Disregulation of prion protein expression alters REM sleep homeostasis in aged mice
Loris Ferrari, *Institute of Human Physiology II - University of Milan Medical School, Milan, Italy*

7 Experience-dependent structural and functional plasticity of auditory-motor systems in the human brain
Emily Coffey, *Z-Lab, McGill University, Montreal, Canada*

8 Differential electrodermal and phasic heart rate responses to personally relevant information-Comparing sleep and wakefulness
Gordon Benedikt Feld, *Institute for Neuroendocrinology, University Medical Centre Schleswig-Holstein, Lübeck, Germany*

9 The molecular basis of prion toxicity - Transcriptomics in an organotypic slice model
Uli Simon Herrmann, *Sleep disorders centre, University Hospital Inselspital, Bern, Switzerland*

10 Dissociable consequences of memory reactivation during sleep and wakefulness
Susanne Diekelmann, *Department of Neuroendocrinology, University of Lübeck, Germany*

11 Associations between diurnal preference, sleep quality and externalising behaviours in young adults: A behavioural genetic analysis
Nicola Barclay, *Goldsmith's University of London, United Kingdom*

12 A non-invasive, high-throughput approach for the assessment of sleep in mice in response to pharmacological and environmental manipulation
Simon Fisher, *Nuffield Department of Opthalmology, University of Oxford, United Kingdom*

13 Anxiety-impaired sleep quality enhances homeostatic sleep pressure
Vladimira Jakubcakova, *Max-Planck-Institute of Psychiatry, Munich, Germany*

14 Changes in cardiovascular parameters during REM sleep in rats exposed to different ambient temperatures
Davide Martelli, *Dept. of Human and General Physiology, University of Bologna, Italy*

15 Sleep Does not Affect Binding Process in Episodic Memory
Sophie Galer, *Erasmus Hospital, University Lebre de Bruxelles, Belgium*

16 Spatial cognition of animals and humans based on abstract spatial stimuli - Model for higher cognitive function
Tereza Nekovarova, *Departement of Neurobiology of Memory and Computational Neurosciences, Institute of Physiology, Czech Academy of Sciences, Prague, Czech Republic*

17 Event-related activity and phase locking during a psychomotor vigilance task
Kerstin Hödlmoser, *Dept. of Psychology, University of Salzburg, Salzburg, Austria*

18 Is the temperature in your bed related to sleep onset
Tim Weysen, *Philips Research, Eindhoven, The Netherlands*

h 14.30-16.00: <u>Blitz session IV. *Clinical research* (Fürstenzimmer)</u>

Chairs: **Samson Khachatryan** *(Yerevan)*
Burcu Oktay *(Ankara)*
Co-Chair: **Dieter Riemann** *(Freiburg)*

1 Serum levels of MMP-9, sRAGE, hsCRP and Cu can be used as predictive biochemical parameters related to oxidative stress in obese patients with obstructive sleep apnea
Jana Volna, *Department of Neurology, Charles University, 1st Medical Faculty, Praha 2, Czech Republic*

2 Sleep Patterns in Hallucinating Parkinsons Disease Patients and in High-Prone Normal Individuals
Ksenija da Silva, *Department of Biopsychology, University of Primorska, Koper, Slovenia*

3 Light effects on sleep, activity and daytime mood in older people with sleep problems
Katharina Lederle, *Faculty of health and Medical Sciences, University of Surrey, Guildford, United Kingdom*

4 Obstructive Sleep Apnea-Hypopnea Syndrome (OSAHS) diagnosis by human voice analysis. Preliminary Results
Marta Fernandez-Bolanos, *Hospital Txagorritxu, Multidisciplinary Sleep Disorders Unit, Vitoria Spain*

5 Contribution of adenosine related genes to the risk of depression with disturbed sleep
Natalia Gass, *Institute of Biomedicine, Univesity of Helsinki, Helsinki, Finland*

6 Is obstructive sleep apnea associated with REM-sleep behaviour disorder in patients with idiopathic Parkinson's disease?
Eva Breuer, *Dept. of Neurology, Charité - University Medicine Berlin, Germany*

7 Severity of diabetic control is positively correlated with an increased risk of having OSA
Peter Fsadni, *Sleep Laboratory, Division of Respiratory Medicine, Dept. of Medicine, Mater Dei Hospital, Msida, Malta*

8 Centre of Reference for Rare Hypersomnias, a great opportunity for physicians and patients.
Caroline Gauriau, *Centre du Sommeil et de la Vigilance, Centre de Référence Hypersomnies Rares Hôpital de l'Hôtel-Dieu, Paris, France*

9 Experience of sleep laboratory from cluj napoca, romania, in treating patients with obstructive sleep apnea syndrome
Loredana Elena Rosca, *Clinical Hospital of Pneumology "Leon Daniello", Cluj Napoca, Romania*

10 Hypersomnia associated with depression
Cecilia Jara Opazo, *Sleep Center, Dept. of Psychiatry and Psychotherapy, University of Regensburg, Germany*

11 Ventilation limitation during exercise in men with obstructive sleep apnoea
Guoda Pilkauskaite, *Kaunas Medical University Hospital, Kaunas, Lithuania*

12 Indications of mandibular advancement ortheses in the treatement of excessive daytime sleepiness caused by positional supine apnea
Irina Andreea Latu, *UMF Gr. T. Popa Internat Centre Hospitalier, Beziers, France*

13 Impaired glucose tolerance in sleep disorders
Marietta Keckeis, *Max-Planck Institute for Psychiatry, Munich, Germany*

14 Lifetime prevalence of parasomnias and nocturnal behaviours in a sleep clinic population: preliminary finding
Marie-Emmanuelle Beitinger, *Max Planck Insitute of Psychiatry, Munich, Germany*

15 REM and NREM sleep contributions in post-training consolidation of declarative memory. An investigation in narcolepsy and idiopathic hypersomnia
Gaetane Deliens, *Campus du Solbosch, CP 191, Fac. Of Psychological and Educational Sciences, Universite Libre de Bruxelles, Belgium*

h 16.00-16.30: *Coffee break*

h 16.30-17.45: Career Development. *How to write/review a scientific paper* *(Festsaal)*

Chairs: **Derk-Jan Dijk** *(Guildford),* **Malcolm Von Schantz** *(Guildford)*
Discussants: **Lino Nobili** (*Milan*), **Teresa Paiva** (*Lisbon*)

h 17.45-19.30: Official social session I. *Sports and games*

Organizing committee: **Debra J. Skene** (*Guildford*), **Maria Wiechmann** (*Regensburg*)

h 20.30: *Dinner*

h.21.30: Official social session II. *Music and dancing*

Organizing committee: **Margot Mittermeier** (*Ingolstadt*), **Philippe Peigneux** (*Bruxelles*), **Tarja Porkka-Heiskanen** (*Helsinki*), **Maria Wiechmann** (*Regensburg*)

Monday, July 5th

h 7.30-8.30: *Breakfast*

h 8.30-9.45: Round table II. *Ethical issues in human sleep studies* (Festsaal)

Chairs: **Philippe Peigneux** (*Bruxelles*), **Dirk Pevernagie** (*Heeze*)
Discussants: **Joan Santamaria** (*Barcelona*), **Debra J. Skene** *(Guildford)*

h 8.30-9.45: Round table III. *Ethical issues in animal sleep studies* (Fürstenzimmer)

Chairs: **Roberto Amici** (*Bologna*), **Irene Tobler** (*Zurich*)
Discussant: **Pierre Hervé Luppi** (*Lyon*)

h 9.45-10.45: Keynote lecture III. *Chronic insomnia - challenges for the future* (Festsaal)

Dieter Riemann (*Freiburg)*
Introduced by: **Thomas Pollmächer** (*Ingolstadt*)

h 10.45-11.15: *Coffee break*

h 11.15-13.00: Oral session III . *Cinical research* (Festsaal)

Chairs: **Marietta Keckeis** *(Ingolstadt)*
Kiril Terziyski *(Plovdiv)*
Co-Chair: **Thomas Pollmächer** (*Ingolstadt*)

1 HPA axis function in primary insomnia, sleep apnea and restless legs syndrome
ZuzanaLattova, *Zentrum für psychische Gesundheit, Klinikum Ingolstadt and Max Planck Institute of Psychiatry Munich, Germany*

2 Lack of sleep-dependent spatial memory consolidation in post-traumatic stress disorder survivors of the 2009 L'Aquila earthquake
Daniela Tempesta, *Laboratory of Sleep, Faculty of Psychology, University of L'Aquila, Italy*

3 REM sleep increase after acute deep brain stimulation of the subgenual cingulate gyrus in patients with treatment resistant depression
Claire Durant, *Psychopharmacology Unit, University of Bristol, United Kingdom*

4 Do you sleep regularly-A new algorithm to determine sleep variability in sleep diaries
Thomas Unbehaun, *Department of Psychiatry, University of Freiburg, Germany*

5 Secondary hypogonadism induced by severe obstructive sleep apnea syndrome (OSAS) and results after two months CPAP treatment
Raluca Mihaela Bercea, *Clinic of Pulmonary Diseases, Iasi, Romania*

6 A Neuropsychological Study of Executive Functions in Chronic Insomnia
Christina Ilioudi, *Universidad Autonoma de Madrid, Spain*

7 Contrasting gray and white matter changes in preclinical Huntington disease- An MRI study
Diederick Stoffers, *Netherlands Institute for Neuroscience, Amsterdam, The Netherlands*

8 Sleep disturbances as a predictor of cause-specific work disability and delayed return to work
Paula Salo, *Unit of Excellence for Psychosocial Factors Finnish Institute of Occupational Health, Turku, Finland*

h 13.00-14.30: *Lunch*

h 14.30-16.00: Blitz session V. *Basic Research* (Festsaal)

Chairs: **Tristan Bekinschtein** *(Cambridge)*
Sophie Galer *(Bruxelles)*
Co-Chair: **Roberto Amici** *(Bologna)*

1 Sleep and metabolism - sleep regulation in a USF1 knockout mouse mode
Kirsi-Marja Rytkönen, *Institute of Biomedicine, Dept. of Physiology, University of Helsinki, Finland*

2 The effects of 40 hours of sleep deprivation and recovery night on circadian profile of human immune cells
Bojan Rojc, *University Clinical Center, Ljubljana Institute of Clinical Neurophysiology, Izola, Slovenia*

3 Sleep-dependent memory consolidation in young healthy subjects - a fMRI study
Caroline Harand, *Research Unit U923, Inserm-EPHE-University of Caen, France*

4 Fingerprinting the sleep-related memory processing in the EEG spectra
Ana Jeronci´c, *Faculty of Natuaral Science, Mathematics and Kinesiology, University of Split, Croatia*

5 Altered Body Temperature Rhythm and Depression-like Symptoms following Early and Later Life Stress in Rats
Janne Gronli, *Dept of Biological and Medical Psychology, University of Bergen, Norway*

6 Networks within and between the basal forebrain, hippocampus and prefrontal cortex - in a model for depression caused by disturbed sleep
MarkusLagus, *Institute of Biomedicine, Sleep Research Lab., University of Helsinki, Finland*

7 Sleep-dependent daily changes in blood pressure in leptin-deficient obese mice
Viviana Carmen Lo Martire, *Dept. of Human and General Physiology, University of Bologna, Italy*

8 Effect of sleep deprivation on neurochemical status in the rat basal forebrain in clomipramine model of depression
Sergey Savelyev, *Dept of Neuroscience, Karolinska Institute, Stockholm, Sweden*

9 The effects of neurofeedback on memory performance and sleep
Doris Moser, *Dept. of Neurology, Medical University of Vienna, Austria*

10 Overt replay of a recently learned motor sequence during human slow-wave sleep in sleepwalkers
Delphine Oudiette, *Pathologies du sommeil, Hôpital Pitié-Salpêtrière, Paris, France*

11 Positive effects of Red Bull® Energy Drink on driving performance during prolonged driving
Monique Mets, *Utrecht University, The Netherlands*

12 Sleep changes under condition of modeling of longtime space mission
Irina Rusakova, *Seventsov Institute, Russian Academy of Sciences, Moscow, Russian Federation*

13 Sensing the future: skin temperature predicts lapses in vigilance
Nico Romeijn, *Netherlands Institute for Neuroscience, Amsterdam, The Netherlands*

14 The characteristics of sleep during early period of pregnancy in rats
Elizaveta Rutskova, *Institute for Higher Nervous Activity and Neurophysiology, Moscow, Russian Federation*

15 WAY-100635 attenuates phrenic long term facilitation in rats
Ivana Pavlinac, *School of Medicine, University of Split, Croatia*

16 Sleep, mood and emotional processing
Kate Porcheret, *Nuffield Laboratory of Opthalmology, John Radcliffe Hospital, University of Oxford, United Kingdom*

17 A nap - as good as a night
Annedore Pawlizki, *Allgemeine und Experimentelle Psychologie, LMU München,Munich, Germany*

h 14.30-16.00: <u>Blitz session VI. *Clinical Research* *(Fürstenzimmer)*</u>

Chairs: **Andras Szentkiralyi** *(Budapest)*
Mónica Vicente *(Montpellier)*
Co-Chair: **Patrick Levy** *(Grenoble)*

1 Polisomnographycs results in Chiari malformation I
Alex Ferre, *Hospital Universitario Vall d'Hebron, Barcelona, Spain*

2 Restless legs syndrome in patients with multiple sclerosis - epidemiology and genetics
Jana Vavrova, *Department of Neurology, Charles University and General University Hospital, Praha 2, Czech Republic*

3 Heart rate and heart rate variability in primary insomnia
Kai Spiegelhalder, *Dept of Psychiatry and Psychotherapy, University of Freiburg Medical Center, Freiburg, Germany*

4 Is the two hour recommended maximum driving time appropriate for both healthy older and treated obstructive sleep apnoea drivers?
Ashleigh Filtness, *Loughborough University, United Kingdom*

5 The lowest desaturation in patients with sleep apnea syndrome
Stefan Marian Frent, *Victor Babes Clinical Hospital of Pneumology and Infectious Diseases, Timisoara, Romania*

6 Influence of microarousals on subjective sleep quality
Raminta Masaitiene, *Sleep Disorder Laboratory, Sapiega Hospital, Vilnius, Lithuania*

7 Motor-behavior during REM sleep of narcoleptic with cataplexy patients -a systematic classification
Christian Franceschini, *Department of Neurological Science, University of Bologna, Italy*

8 Evaluation of P wave dispersion, QT dispersion and P wave amplitude in patients with obstructive sleep apnea syndrome
Burcu Oktay, *Diskapi Yildirim Beyazit, Training and Research Hospital, Ministry of Health, Ankara Turkey*

9 Non-invasive measurements of respiratory effort
Nele Vandenbussche, *Centrum voor slaapgeneeskunde Kempenhaeghe, Heeze, The Netherlands*

10 Correlation Between Cyclic Alternating Pattern Parameters And Subjective Daytime Sleepiness Scores
Petar Petrov, *Sleep Lab, Mana Medical Centre, Sofia, Bulgaria*

11 Sleep, daily PER2 expression and melatonin secretion levels - findings from patients and healthy controls
Bogdan Ioan Voinescu, *Department of Physiology, University of Medicine and Pharmacy, Cluj-Napoca, Romania*

12 Sleep-disordered breathing and paroxysmal nocturnal behaviours in extrapyramidal syndromes - which relationship
Pietro Luca Ratti, *Sleep Medicine and Electophysiology Unit, Istituto Neurologico "C. Mondino", Pavia, Italy*

13 Sleep length, Television and Computer habits and Overweight in Swedish School - Aged Children and Adolescents
Pernilla Garmy, *Department of Health Scienses, Lund, Sweden*

14 The role of personality traits in insomnia
Merijn van de Laar, *Kempenhaeghe, Centre for Sleep Medicine, Heeze, The Netherlands*

15 Sleep and temperature in Alzheimers disease and healthy controls
Els Most, *Medical Centre, VU University, Amsterdam, The Netherlands*

h 16.00-16.30: *Coffee break*

h 16.30-17.00: Special session: *Sleep research and sleep medicine in China* *(Festsaal)*

Xiangdong Tang *(Chengdu*)

h 17.00-18.00: Oral session IV. *Basic research* *(Festsaal)*

Chairs: **Simon Fisher** *(Oxford)*
Johanna Schwarz *(Stockholm)*
Co-Chair: **Malcolm Von Schantz** (*Guildford*)

1 Effects of light supplementation on self-rated depression and sleep quality in older people living in care homes
Samantha Hopkins, *Faculty of Health and Medical Sciences, University of Surrey, Guildford, United Kingdom*

2 Influence of daytime light on nighttime parameters like sleep, melatonin secretion and alertness
Claudia Stoll, *Department of Sleep Medicine, Charité University Hospital Berlin, Germany*

3 Social effects on circadian behavior in ant
Stéphane Dorsaz, *Center of Integrative Genomics, University of Lausanne, Switzerland*

4 Sleep homeostasis in the rat during chronic sleep restriction
Susan Leemburg, *Schlaflabor, Neurologische Klinik, Universitätsspital Zürich, Switzerland*

5 Double knockout mice lacking histamine and orexins-a full model of narcolepsy for physiopathological and therapeutic studies
Koliane Ouk, *Integrated Physiology of Brain Arousal Systems, Claude Bernard University, INSERM/UCBL-U628, Lyon, France*

h 18.00-19.00: Final exam *(Feestsaal)*

h 20.30: *Dinner*

Tuesday, July 6th

h 7.30-8.30: *Breakfast*

h 8.30-9.30: **Blitz session VII. *Basic Research* (*Festsaal)***

Chairs: **Marija Bakotic** *(Zagreb)*
Uli Simon Herrmann *(Bern)*
Co-Chair: **Zoran Dogas** *(Split)*

1 Task-induced neuronal network connectivity reappears during sleep in humans
Giovanni Piantoni, *Netherlands Institute for Neuroscience, Amsterdam, The Netherlands*
2 Differential item functioning in the Epworth Sleepiness Scale using two psychometric approaches
Martin Ulander, *Dept of Clinical Neurophysiology, Linköping University, Hospital Linköping, Sweden*
3 Sleep deprivation fails vanishing pseudoneglect
Rémy Schmitz, *Faculty of Psychological Sciences, Universite Libre de Bruxelles, Belgium*
4 Electrophysiological correlates of processing aversive experiences in an animal model
Stephanie Polta, *Neuronal plasticity, Max Planck Institute of Psychiatrie München, Germany*
5 Association between lunar phase and sleep characteristics
Csilla Zita Turanyi Madarasz, *Institute of Behavioural Sciences, Semmelweis University, Budapest, Hungary*
6 Investigation on the signalling pathways controlling Arc protein expression after cholinergic activation in SH-SY5Y neuroblastoma cells and cultured hippocampal slices
Jonathan Soule, *Biomedicine, University of Bergen, Norway*
7 Stimulation of anterior cingulate gyrus and modulation of pain
Elena Lainez, *University Vall de Hebron Hosptial, Barcelona, Spain*
8 The influence of pre-sleep cognitive arousal on sleep onset processes
Johan Wuyts, *Biological Psychology, Vrije Universiteit Brussel, Mechelen, Belgium*
9 Linking Sleep - Behaviour and Cognition in Childhood - a Meta-Analysis
Rebecca Schutte, *Netherlands Institute for Neuroscience, Amsterdam, The Netherlands*
10 Sleep and EEG effects of gamma-hydroxybutyrate, baclofen and GABAB receptor subunits
Julie Vienne Bürki, *Centre for Integrative Genomics, University of Lausanne, Switzerland*
11 Neuroanatomical Sleep-Dependent Processing in the Probabilistic Serial Reaction Time Task
Charline Urbain, *Faculty of Psychological Sciences, Universite Libre de Bruxelles, Belgium*

h 8.30-9.30: **Blitz session VIII. *Clinical Research* *(Fürstenzimmer)***

Chairs: **Ashleigh Filtness** *(Loughborough)*
Elias Karroum *(Paris)*
Co-Chair: **Teresa Paiva** *(Lisbon)*

1 Chronotropic parameters from cardiopulmonary exercise testing in patients with severe obstructive sleep apnea – preliminary results
Kiril Terziyski, *Medical University of Plovdiv, Bulgaria*
2 Approaching CPAP adherence through a visual analog scale
Joana Teixeira, *Hospital Pulido Valente, Lisbon, Portugal*
3 Chronotypes and subjective sleep parameters in epilepsy patients: a large questionnaire study
WytskeHofstra, *Epilepsy and Sleep Center SEIN, Zwolle, The Netherlands*
4 Cardiovascular risk in patients with moderate and severe obstructive sleep apnea syndrome
Gianina Rusu, *Centre Integratif de Genomique (CIG), Universite de Lausanne, Switzerland*
5 Determinants of REM sleep without atonia in narcolepsy-cataplexy
MónicaVicente, *Unité de Troubles du Sommeil et l'eveil CHRU Gui de Chauliac, Montpellier, France*
6 Cardiovascular responses in preterm infants at 34-39 weeks of conceptual age
Suvi Viskari-Lähdeoja, *Hospital for Children and Adolescents, University of Helsinki, Espoo, Finland*
7 Performance of different evaluation scales of neurocognitive function in Sleep Apea Syndrome
Roxana-Elena Stanciu, *Clinic of Pneumology at University of Medicine, Timisoara, Romania*

8 Sleeping habits and sleep disorders prevalence in infants aged 6 and 15 months
Carmen Soria Bretones, *Hospital Virgen de la Luz, Cuenca, Spain*

9 Evolution of objective, subjective and EEG measures of vigilance in patients with idiopathic hypersomnia during 40 hours prolonged wakefulness
Katharina Hefti, *Institute of Pharmacology and Toxicology, University of Zurich, Switzerland*

10 The amount of deep sleep is inversely related to daytime systolic blood pressure in patients with chronic kidney disease
Andras Szentkiralyi, *Institute of Behavioural Sciences, Semmelweis University, Budapest, Hungary*

h 9.30.10.30: Oral session V. *Basic research* *(Festsaal)*

Chairs: **Sebastian Holst** *(Zurich)*
Alison Mary *(Bruxelles)*
Co-Chair: **Debra J. Skene** (*Guildford*)

1 Disruption of Sleep by Sound is Predicted by Spindle Density in Humans
Thien Thanh Dang-Vu, *Division of Sleep Medicine, Dept. of Neurology, Massachusetts General Hospital/Harvard Medical School, Boston, USA*

2 Dynamic changes in neurotransmitter levels in the basal forebrain during and after sleep deprivation
Janneke Zant, *Institute of Biomedicine, University of Helsinki, Finland*

3 Memory Consolidation During a Daytime Nap
Simone Duss, *Department of Psychology (Division of Experimental Psychology and Neuropsychology, University of Bern, Switzerland*

4 Benefits of napping and an extended duration of recovery sleep on alertness and immune cells after acute sleep restriction
Brice Faraut, *Unit 222, Sleep Research Laboratory, Universite Libre de Bruxelles, Montigny-Le-Tilleul, Belgium*

5 Sleep disturbance impedes stroke recovery in the rat
Cristina Zunzunegui , *Dept. of Neurology, University Hospital of Zurich, Switzerland*

h 10.30-11.00: *Coffee break*

h 11.00-12.00: General discussion and farewell

h 12.00-13.00: *Lunch*

Abstracts

Current study on sleep quality assessment in Georgian general population

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Georgian Sleep Research and Sleep Medicine Society, Tbilisi, Georgia
Research-Practical Center for Prevention and Control of Epilepsy, Tbilisi, Georgia

Introduction: It is well-known that sound sleep is important for health and well-being, professional relationships, public safety and productivity. Over the last decades, there has been devoted a great attention to sleep-related problems' dissemination in different population. Compared with western countries, there has not been conducted complete population-based study concerning sleep quality assessment in Georgia. Therefore this study was aimed to begin the investigation of sleep quality of Georgian general adult population through the conducting of questionnaire study.

Participants and Methods: 456 individuals (females and males), aged 18-63 years (mean age 35.4) were asked to complete a comprehensive self-report questionnaire with 22 items assessing sleep-wake habits, sleep symptoms and demographic status. Each subject filled out the Pittsburg Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS).

Results: Preliminary data indicate that 62.3% of total sample has one or other symptom of sleep problems such as sleep onset difficulty (more than 30 min is needed for falling asleep) and/or frequent nocturnal awakenings. Most of these subjects are not satisfied with the quality of their nocturnal sleep. It has been noted that the most of questioned subjects have not focused their attention on sleep problems before and few think they have sleep disturbances. Descriptive findings of this study allow us to suggest that today Georgian youth has no less sleep-related problems than aged people. Only about one-half of respondents are able to say that on most nights per week they have a good night's sleep without excessive daytime sleepiness.

Conclusion: Preliminary findings of the present study show that the inhabitants of Georgia have different sleep-related problems. It is signified the need to continue longitudinal population-based research on the sleep quality investigation in Georgia through the recommendations of the European experts involved in the field of clinical sleep research and sleep medicine.

Hyperarousal in insomnia: fact or fiction?

Ellemarije Altena
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Recently, a growing body of literature focused on the feature of hyperarousal causing, maintaining or being the consequence of insomnia. Hyperarousal can be subdivided in physiological, cortical and cognitive hyperarousal, each of which may play their own role in the onset, maintenance and consequences of this condition. I will present some of our recent neuroimaging data that could show proof of this subdivision. Though some features of insomnia are sensitive to short term interventions such as cognitive behavioural therapy, some other striking physiological differences do not respond to this therapy whatsoever. Is this proof of the trait of insomnia? Are you born with this and just have to live with it? Or is it just an expression of a very different underlying mechanism, perhaps even primarily unrelated to insomnia? Suggestions of how to design future studies to map this condition are given in more detail.

Influence of sleep depth in an afternoon nap on the capacity to learn new information

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Objectives: According to the consolidation theory, sleep helps to establish memories for things in the past. Slow wave sleep (SWS) is associated with the consolidation of declarative memories. In addition, the synaptic downscaling theory stresses the importance of sleep before encoding of new memories for the formation of these memories. In particular SWS might affect the encoding of new information afterwards. In our study, we investigate the influence of the amount of SWS before the learning of new information on subsequent encoding performance.

Methods: Herein, we aim at deepening sleep (i.e., increasing the amount of SWS) by a mild electrical current (transcranial direct current stimulation [tDCS]) during an afternoon nap and investigate the effects of this manipulation, compared to a sham stimulation control condition, on subsequent performance in declarative and non-declarative learning tasks (word pair associates, word lists, pictures, finger tapping).

Expected results: We expect to find an increased encoding performance in declarative learning tasks after a higher amount of SWS compared to the control condition.

Conclusion: This result would support the assumption that SWS before the encoding of new memories is important for the formation of these memories by freeing up capacity to learn new information.

Grouping of MEG gamma band activity by spindles

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b Graduate School for Computing in Medicine and Life Sciences, University of Lübeck, Germany

Objectives. Studies have shown that memory consolidation is strongly related to sleep spindles. Gamma band activity is considered to represent local cortical processing of inter-related memory information. The aim of this study is to investigate whether there is a temporal relation between MEG gamma band activity and sleep spindles.

Methods. An experiment was carried out where seven healthy volunteers slept in supine position while recordings of MEG (151 channels), EEG (FZ, CZ), EMG, and EOG were obtained. Offline sleep scoring was performed according to standard criteria. Spindles were detected in EEG. A spindle epoch is defined to be ±1.4s widow time locked to the spindle peak. The MEG gamma band was subdivided into two sub-bands 25-40Hz (low) and 40-100Hz (high). Time-frequency representation of the biological signal's power was computed using Morlet wavelet time locked to the spindle peak. In order to test if the phase of the spindle modulates the power of MEG, cross-frequency interaction between the phase of the spindles and the time-course of the gamma power was computed using coherence analysis.

Results. Preliminary results reveal that MEG power in the spindle range (12-15Hz) is systematically modulated by EEG spindles. Low gamma band in MEG (right occipital) was found significantly higher in power during the second half of spindle epochs compared to epochs without spindles. The cross-frequency analysis revealed that the phase of the EEG spindles enhances the power of MEG in the low and high gamma bands especially in parietal-occipital and mid-prefrontal cortical areas.

Conclusion. Sleep spindles modulates the power of MEG gamma activity. The findings are consistent with the idea that spindles provide a fine-tuned temporal frame for memory processing during sleep.

Vigilance Impairment in Narcolepsy

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Introduction. Narcolepsy is a sleep-wake disturbance which is characterized by excessive daytime, disturbed night sleep and rapid eye movement sleep-associated symptoms such as cataplexy, hypnagogic hallucination and sleep paralysis.
Compared to excessive daytime sleepiness, impaired vigilance is less evaluated, although it has a direct impact on daily performance and quality of life.
Recent studies suggest using specific tests such as SART (Sustained Attention to Response Task) and PVT (Psychomotor Vigilance Task) for vigilance assessment in narcolepsy. Regarding to the common maintenance of wakefulness test (MWT), SART and PVT are more specific tests on vigilance and not so time consuming.
Sodium oxybate is the first choice treatment for cataplexy and disturbed night sleep in narcolepsy. However, the effect of sodium oxybate on vigilance is not evaluated yet, therefore the aim of our study is to assess the effect of sodium oxybate on vigilance by SART and PVT.

Methods. SART and PVT will be assessed in narcoleptic patients twice (pre- and post therapy) and in gender-/age-matched healthy controls. The whole study protocol involves further measures as actigraphy over two weeks, MWT, OSLER, polysomnography (these data are not presented in this abstract). The vigilance task battery is installed on a PDA and subjects perform tests at home three times a day over a time period of seven days.

Results. At this early stage of the study only preliminary results are available. Four patients have done this test procedure before treatment and one of this four did this test procedure under sodium oxybate. Additionally three healthy controls have been tested so far. Compared to controls narcoleptics are slower and have more lapses on PVT-task (reaction time (RT): (255 ms vs. 379 ms; lapses: 1 vs. 13) and have more errors on the SART-task (5 vs. 7). Treatment shortened RT and decreased lapses (PVT) by 7% and 46%, respectively, however, no improvement could be found on SART (n=1).

Conclusion. It is feasible to measure vigilance by using PVT and SART on a PDA in an ambulatory setting. The treatment with sodium oxybate seems to improve performance on PVT while on SART no improvement can be detected. More patients and controls have to be tested to validate our preliminary results.

Insomnia is a predictor of depression: A meta-analytic evaluation of longitudinal epidemiological studies

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Objectives. In many patients with major depression, symptoms of insomnia herald the onset of the disorder and may persist into remission or recovery, even after adequate treatment. Several studies have raised the question whether insomniac symptoms may not only be signs/symptoms of the disorder, but constitute an independent clinical predictor of depression. However, up to date, no systematic evaluation of such a causal relationship is available. Aim of the present study was to evaluate quantitatively if insomnia constitutes a predictor of depression, by performing a meta-analysis of longitudinal epidemiological studies.

Method. PubMed, Medline, PsycInfo, and PsycArticles databases were searched from 1980 until February 2010 for longitudinal epidemiological studies simultaneously investigating insomniac complaints and depressed symptoms/ psychopathology. We also reviewed references from all retrieved articles. Effects were summarised using the logarithms of the odds ratios for insomnia at baseline to predict depression at follow-up. Studies were pooled with both fixed-effects and random-effects meta-analytic models in order to evaluate the concordance. Heterogeneity test and sensitivity analysis were computed.

Results. Twenty-one studies met inclusion criteria. Considering all studies together, heterogeneity was found. The random-effects model showed an overall odds ratio for insomnia to predict depression of 2.60 (confidence interval [CI]: 1.98-3.42). When the analysis was adjusted for outliers, the studies were not longer heterogeneous. The fixed-effects model showed an overall odds ratio of 2.10 (CI: 1.86-2.38).

Conclusions. The results of the current meta-analysis indicate that non-depressed people with insomnia have a twofold risk to develop depression, compared to people with no sleep difficulties. Thus, early and easy accessible treatment programs for insomnia might reduce the risk for developing depression in the general population and be considered a helpful general preventive strategy in the area of mental health care.

The effects of trait and state activation on daytime sleepiness after partial sleep deprivation

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Objectives. The goal of this study was to test some hypotheses from the model of sleepiness proposed by De Valk and Cluydts (2003). Therefore, we examined the effects of trait and state measures of activation and sleepiness on subjective and objective measures of daytime sleepiness after partial sleep deprivation.

Methods. 28 healthy adults, aged 18-26 years (14 males), spent one night and the following morning in the laboratory. During the night the participants had opportunity to sleep half of their usual sleep time, which was accomplished by delaying their usual bedtime. In the morning they participated in two experimental situations, which differed in the level of activation. The level of activation was manipulated by two laboratory tasks: a simple reaction time task (SRT), and a combined speech and mental arithmetic task (CT). The order of the tasks was balanced between the subjects. Heart rate and electrodermal activity (EDA) were measured before and during each task, and subjective activation and anxiety were estimated before and after the tasks. After each task sleepiness was measured by the Karolinska Sleepiness Scale (KSS) and a single Sleep Latency Test (SLT) based on the MSLT rules. EDA lability during rest was used as a trait measure of activation, and the results on the Epworth Sleepiness Scale (ESS) as a measure of trait sleepiness. Additionally, trait anxiety was measured by the STAI-T Inventory.

Results. Repeated measures ANOVAs and paired t-tests were performed. All objective and subjective measures of activation and anxiety indicated that higher levels of activation and tension were evoked by the CT compared to the SRT. The results on the KSS were lower after performing CT than after SRT (M_{ct}=5.9, sd=1.76; M_{srt}=6.6; sd=1.91). It took longer to fall asleep in the SLT after performing CT than after SRT (M_{ct}=9.6; sd=6.94; M_{srt}=6.2; sd=6.34). None of the trait measures of activation or sleepiness had a significant effect on sleepiness measures.

Conclusion. Increased level of sympathetic activation and subjective tension can decrease subjective sleepiness and linger sleep onset after partial sleep deprivation. These results support the hypothesis about the importance of state activation as one of the determinants of daytime sleepiness, proposed in the model by de Valk and Cluydts. On the other had, the results of this experimental study do not support inclusion of trait aspects of activation or sleepiness in the proposed model.

Associations between diurnal preference, sleep quality and externalising behaviours in young adults: A behavioural genetic analysis.

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Barbara Maughan, *King's College London, Institute of Psychiatry, University of London, UK*
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Alice M. Gregory, *Department of Psychology, Goldsmiths, University of London, UK*

Objectives. Certain sleep phenotypes co-occur with externalising behaviours in youth, yet little is known about these associations in adults. The present study determines the extent to which diurnal preference (morningness vs. eveningness) and sleep quality are associated with externalising behaviours; explores the degree of overlap in the genetic and environmental influences between phenotypes; and examines the extent to which genetic and environmental influences account for the associations.

Methods. Using a twin design, data on diurnal preference (measured by the 'Morningness-Eveningness Questionnaire'), sleep quality (measured by the 'Pittsburgh Sleep Quality Index'), and externalising behaviours (measured by the 'Adult Self-Report') were collected from 420 monozygotic twins, 773 dizygotic twins, and 329 siblings (mode age = 20 yrs, range = 18-27 yrs) from a population-based twin registry across the UK.

Results. There were significant associations between diurnal preference, sleep quality and externalising behaviours (range r = .26-.33) indicating that greater eveningness preference was associated with poorer sleep quality and greater externalising symptoms. Additive genetic overlap between sleep variables and externalising behaviours was moderate (rA = .38-.53). Non-shared environmental correlations were small for all associations (rE = .07-.13). Additive genetic [A] influences accounted for a large proportion of the variance in all associations between phenotypes (range A = 81%-90%). The remaining source of variance was accounted for by non-shared environmental [E] influences (range E = 10%-19%).

Conclusion. A preference for eveningness and poor sleep quality are modestly associated with externalising behaviours in adults. The associations between phenotypes are largely explained by genetic influences and there is moderate overlap in the genes influencing sleep and externalising behaviours. Further research should focus on identifying specific genetic polymorphisms common to diurnal preference, sleep quality and externalising behaviours, since genes already known to influence one phenotype may be worthy candidates for exploration with regards to associated phenotypes.

Sleep entails arterial hypertension in hypocretin-deficient narcoleptic mice

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Objectives. High values of blood pressure (BP) during sleep and reduced difference in BP between sleep and wakefulness carry negative prognostic information. The central neural pathways that regulate cardiovascular changes across behavioral states are still to be investigated. Hypothalamic neurons releasing hypocretin (HCRT) peptides are promising targets of investigation, being involved in the regulation of both wake-sleep cycle and cardiovascular system and being lost in narcolepsy. Aim of this study was to investigate whether lack of HCRT signaling causes derangements in BP during sleep.

Methods. We studied two different models of narcoleptic mice: HCRT-ataxin3 transgenic mice (TG, n=12) in which HCRT neurons were selectively and postnatally ablated by expression of a neurotossic transgene product, and HCRT gene knock-out mice (KO, n=8) in which neurons were preserved but HCRT production was compromised. Wild-type mice (WT, n=10) congenic to both TG and KO were used as control group.
Mice were implanted with a telemetric pressure transducer (TA11PA-C10, DSI) and electrodes for discriminating wakefulness, rapid-eye-movement sleep (REMS), and non-REMS (NREMS). Ten days later, recordings were performed for 3 days with the mice undisturbed and freely moving. Mean BP values were computed in each wake-sleep state and analyzed by ANOVA and t-test with significance at $p<0.05$. Data are reported as mean ± SEM.

Results. Mean BP was significantly higher in both TG and KO than in WT mice during NREMS (4±2 and 7±2 mmHg, respectively) and particularly during REMS (11±2 and 12±3 mmHg, respectively), but not during wakefulness. The physiologic decrease in BP during either NREMS or REMS with respect to wakefulness was lower in both TG and KO than in WT mice.

Conclusion. These results indicate that in narcoleptic mice, lack of HCRT signaling impairs the physiological decrease of BP during sleep, leading to sleep-related neurogenic hypertension. These findings may be relevant to cardiovascular risk in narcolepsy and support the involvement of hypothalamic HCRT neurons in the regulation of BP during sleep.

Lifetime prevalence of parasomnias and nocturnal behaviours in a sleep clinic population: preliminary findings

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Objectives. Parasomnias are undesirable phenomena occurring during sleep and involving skeletal muscle activity (AASM, 2005). Relatively little is known about the frequency of parasomnias or other nocturnal behaviours in psychiatric and even sleep-disordered patients. The Munich Parasomnia Screening (MUPS) is a validated self-rating questionnaire with 21 items assessing the lifetime prevalence and current frequency of parasomnias, various sleep-related movements and nocturnal behaviours in adult persons (Fulda et al, 2008).

Methods. We assessed lifetime prevalence of 21 nocturnal behaviours using the MUPS in a population of patients visiting the clinical sleep laboratory of the Max Planck Institute of Psychiatry in Munich. Specifically, we included 63 sleep-disordered patients without psychiatric disorders (33 females (f), 30 males (m); age 49.3 ± 17.9 years) and 78 sleep-disordered patients with comorbid psychiatric disorders (34 f, 44 m; 47.9 ± 12.9 years). These were compared to 57 narcoleptic patients (26 f, 31 m; 48.9 ± 17.1 years).

Results. Narcoleptic patients reported more often hypnagogic hallucinations (70.2 %), sleep paralysis (57.9 %), and sleep talking (80.7 %) than other sleep-disordered patients independently of a concomitant psychiatric disorder (25.5 %, 12.1 %, and 54.6 %, respectively). In addition, there was a tendency towards a higher frequency of sleep-related eating, violent behaviour during sleep and behaviours suggestive of REM sleep behaviour disorder (RBD) in narcoleptic patients. Sleep-disordered patients with comorbid psychiatric disorders reported more often sleep terror, hypnagogic hallucinations, sleep-related groaning and sleepwalking than patients without psychiatric disorders.

Conclusions. According to the MUPS, narcoleptic patients report an increased lifetime prevalence of various sleep-related behaviours apart from typical hypnagogic hallucinations and sleep paralysis. In addition, sleep-disordered patients with comorbid psychiatric disorders are more likely to report a variety of nocturnal behaviours. Whether this is due to the psychopharmacological medication remains to be determined.

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Glucose Tolerance in Patients with Narcolepsy

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Objectives. Increased body weight is a common feature of narcolepsy. In addition, an increased occurrence of non-insulin dependent diabetes has been reported. So far, it is not known whether glucose metabolism in narcolepsy is disturbed due to, or independently of obesity.

Methods. We studied 17 patients with narcolepsy/cataplexy and 17 healthy controls matched for age, sex and body mass index (BMI) in a case-control design. A 75g oral glucose tolerance test was performed in all.
We assessed glucose tolerance by means of the glucose curve during oral glucose challenge from 0 to 240 minutes; insulin sensitivity and insulin secretion by homeostasis model assessment and minimal model analysis; basal HbA1c, TSH, and cholesterol levels.
Analyses were undertaken for the complete group and for a subgroup of eight patients and controls that were individually matched for BMI with the aim to identify a narcolepsy specific risk that is independent of overweight.

Results. For the complete group standard endocrine measures and indices of the oral glucose tolerance test did not differ between and controls. However, when comparing the subgroup of eight patients and controls that were individually matched for BMI mean glucose level at 120 minutes and area under curve were significantly lower in patients (P=0.01 and P=0.02, respectively).

Conclusions. On a group level and controlling for BMI, we found no difference in glucose metabolism between narcoleptic patients and controls. However, in a subgroup of BMI-equivalent cases and controls we observed a flattening of glucose clearance in patients which suggest subtle weight-independent abnormalities of glucose metabolism. Nevertheless our results draw the focus of interest back to the narcolepsy inherent overweight and point to weight management as the most promising clinical route to improve glucose metabolism in narcolepsy patients.

Losing consciousness: falling asleep during a go/no-go task

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We aimed to map the EEG-ERP and behavioural pattern changes from fully awake, to drowsy, to sleep stage 1 and 2 in a decision-making task. We asked a group of subjects to press a button to a series of tones (go-left) and a different button to other tones (go-right). There were also tones that required the subjects to take no action (no-go trials). Preliminary analysis showed that reaction times got longer and more variable when going from full wakefulness to drowsiness. The evoked response to the tones became stronger in sleep stage 1, and the preparation/decision potential changed morphology but still showed differences between go and no-go trials. Stage 2 showed no button press responses but there were still some lateralized potentials to the left hand and right hand tones. The pre-trial signal predicted the subsequent motor response for most of the trials. On the basis of these preliminary findings, we believe that decision making depends on conscious control and it is still, to a certain extent, spared in sleep Stage 1 but appears inconsistent and heavily dependent on the conscious microstate (pre-trial state). We believe there was a tone-hand association consolidated during wake and stage 1 showing no decision related processes in stage 2, nevertheless a memory trace was “on hold” since when the subjects emerged form sleep they reinitiated the task spontaneously.

References.

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Secondary hypogonadism induced by severe obstructive sleep apnea syndrome (OSAS) and results after two months CPAP treatment

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Aim.. OSAS is frequently associated with hypogonadism and decreased libido. Our aim was to determinate the association of androgen deficiency on those patients and to show the CPAP treatment role on correction of androgen deficiency in men diagnosed with OSAS. Also we follow the impact over the life's quality and sexual activity.

Method. We selected 40 patients with severe OSAS after a full night polisomnography. Only 24 subjects agreed to continue with CPAP treatment. We determined the total serum testosterone level (TTR) and the serum luteinizing hormone level (LH) performed in the morning using chemiluminescence's method at baseline and after two months of CPAP. All patients fulfilled Beck Depression Inventory (BDI).

Results. The mean level of TTR was 3,15±0,93 ng/ml considered the hypogonadal level according to guidelines (normal ranges 3,44 -7,72 ng/dl). Mean LH level was 6,00±3,91 U/L (all LH values were in normal ranges or lower). The mean of ages was 50,95±9,3 years old. At baseline we found a negative correlation between TTR and apnea hypopnea index (AHI) ($p=0,0002$, $r=-0,69$), oxygen desaturation index (ODI) ($p=0,0074$, $r=-0,53$), microarousals ($p<0,0001$, $r=-0,87$) and BDI ($p=0,0006$, $r=-0,64$); a positive correlation with noctural degree of oxygenation (SpO2min) ($p=0,0084$, $r=0,52$). After two months with CPAP the mean level of TTR was 3,81±0,47 ng/dl and mean LH level was 6,57±2,73 U/L. We noticed an improve in positive responses to Beck Depression Inventory (from 58,3% at baseline to 45,8% after CPAP) and in positive response to question no 21 referring to sexual activity of BDI.

Conclusions. Our findings suggest that OSAS in men is associated with androgen deficiency and secondary hypogonadism. We noticed that CPAP treatment improves TTR and LH level with positive impact on depressive and libido status of the study group.

Key words: OSAS, testosterone, libido, CPAP

Sleep-related derangements of central autonomic and baroreflex control of heart period in leptin-deficient obese mice

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Objectives. The relationship between heart period (HP) and systolic blood pressure (SBP) reflects the integration between central autonomic and baroreflex control. Aim of this study was to investigate whether leptin deficiency leads to derangements of the central autonomic and the baroreflex control of HP in different behavioural states: wakefulness (W), non-rapid-eye-movement (non-REM) sleep, and REM sleep.

Methods. Experiments were performed on male B6.V-Lep$^{ob/ob}$/OlaHsd obese mice (*ob/ob*, n = 7), which are congenitally leptin-deficient and massively obese, and lean wild type littermates (+/+, n = 11). Mice were implanted with a telemetric blood pressure transducer (TA11PA-C10, DSI) and electrodes for discriminating wake-sleep states. The cross-correlation function (CCF) between the low-frequency (< 0.8 Hz) fluctuations of HP and those of SBP was computed in episodes of W, non-REM sleep, and REM sleep of duration > 60s. The central autonomic and baroreflex contributions to HP control were estimated from the minimum and maximum values of the CCF, respectively. Data were analysed with a 2-way analysis of variance and t-test and significance at $p < 0.05$.

Results. The baroreflex contribution to HP control was significantly lower in *ob/ob* than in +/+ mice during W and non-REM sleep. In *ob/ob* mice, the central autonomic contribution to HP control was preserved during W, whereas it was significantly lower than in +/+ mice during non-REM sleep and REM sleep.

Conclusion. These data indicate a dysregulation of central autonomic and baroreflex cardiac control in leptin-deficient and obese *ob/ob* mice. Moreover, results support the view that pathological derangements of central autonomic and the baroreflex control of HP may be masked or enhanced during different wake-sleep states because of the physiological impact of sleep on cardiovascular regulation.

Is obstructive sleep apnea associated with REM-sleep behaviour disorder in patients with idiopathic Parkinson's disease?

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Objective. Over the past year a variety of sleep disorders have been associated with idiopathic Parkinson's disease (IPS). While there is agreement that REM-sleep behavioural disorder (RBD) is an early clinical manifestation of IPS, it has been controversially debated whether patients with idiopathic Parkinson's disease (IPS) are prone to develop obstructive sleep apnea (OSA). A recently published study in IPS patients with and without disturbed sleep (Cochen de Cock, 2009) found a higher apnea-hypopnea-index (AHI) – as an expression of OSA – in IPS patients with RBD than in those IPS patients without RBD. In line with this observation we are examining the prevalence of OSA in insomniac IPS patients with and without RBD to compare both groups regarding further clinical and polysomnographic parameters as well as regarding the echogenicity of the substantia nigra (SN).

Methods. So far, we have examined 20 patients with IPS (12 male; age: 66.9±6.6) with an insomnia severity index (ISI) >14. All patients underwent video-polysomnography for four nights. The diagnosis of RBD was only established if movements in REM did not emerge from respiratory arousals. An AHI of >5 established the diagnosis of OSA. Transcranial ultrasound was performed using a phased array ultrasound system equipped with a 2.5 MHz probe (Sonoline® Antares system Siemens AG, Germany). In addition we assessed the extent of daytime sleepiness (Epworth sleepiness scale, ESS), the severity of insomnia (ISI), the degree of motor symptoms (UPDRS-part III) and the body mass index (BMI).

Results. 12 patients with IPS (9 male) exhibited RBD all of whom had an apnea-hypopnea-index (AHI) >5/h (mean AHI: 23.3±13.5/h; AHI <5 n=1, AHI: 5-14.9/h n=3, AHI: 15-29.9/h n=4, AHI: >30/h n=4). Conversely, patients with IPS without RBD (n=8, 3 male) had an AHI of 4.6±3.7/h. Patients with IPS and RBD had their apneas/hypopnea equally distributed across non-REM and REM sleep, however a rise of AHI in the supine position was to be noticed. IPS patients with and without RBD did not differ as to echogenicity of SN, BMI, ISI, UPDRS-part III or age ($p>0.05$). Only the mean ESS differed significantly between the tow groups. The mean ESS was significantly higher in IPS patients with RBD ($p <0,5$).

Discussion. Our preliminary data suggest that OSA in insomniac patients with IPS is associated with RBD, but that OSA can only partially explain insomnia in these patients. As apneas/hypopneas equally occur in REM as well as in non-REM sleep OSA does not constitute another manifestation of disturbed REM sleep. Thus the pathophysiology of the association between OSA and RBD still remains to be elucidated. However, this association seems to develop independently from dopaminergic transmission as patients with and without RBD did not differ in view of the severity of motor symptoms related to IPS nor regarding the echogenicity of the SN.

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Sleep and Environmental Context: Interactive Effects for Memory

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Objectives. A rapidly expanding literature has, and continues to demonstrate the importance of sleep for declarative memory consolidation (Born, Rasch, & Gais, 2006). Moreover, memory performance has shown to be improved when an environmental context present at learning is reinstated at retrieval. This effect occurs across, visual (Godden & Baddeley, 1975), auditory (Smith, 1985) and olfactory modalities (Parker, Ngu, & Cassaday, 2001). The present study sought to investigate how these factors may interact.

Methods. A within subjects design was used with retrieval context (same/different as encoding) and retention type (sleep/wakefulness) as factors. Thus, subjects learned a word list in each of two rooms which differed in terms of size, odour and background music. After a twelve hour retention phase containing sleep or only wakefulness (dependent on whether learning took place in the morning or evening) memory was tested using a 'category cued recall' task in one of the learning rooms.

Results. The results demonstrated a significant interaction between context and retention type ($p = 0.01$). A non-significant increase in forgetting was found after a retention period of sleep relative to wake ($p = 0.26$). Conversely, when learning and retrieval contexts were different, significantly more words were forgotten after wake than after sleep ($p = 0.01$). This indicates that an absence of contextual retrieval cues may only negate memory performance when sleep does not follow learning.

Conclusion. Contextual elements of declarative memory representations are thought to rely on the hippocampus (Hoscheidt, Nadel, Payne, & Ryan, 2010). Accordingly, it is possible that across sleep a potential transfer of retrieval dependency from the hippocampus to the neocortex causes a 'decontextualisation' of declarative representations. Consequently, contextual cues may no longer be important for retrieval during the proceeding wakefulness.

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Study of the role of metabotropic glutamate receptors mGlu5 and mGlu7 on sleep and wakefulness in the rat

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Objectives. Glutamate extracellular levels vary across vigilance states being lower during Slow Wave Sleep (SWS) than during Wakefulness (W) and Rapid Eye Movement Sleep (REMS) in several areas of the rat brain. Microinjection of glutamate during W into the rat pedunculopontine tegmentum induced REMS, but the mechanisms underlying these effects are unknown. Recently, a role for metabotropic glutamate receptors mGlu2/3 has been suggested [1, 2]. The main purpose of this study is to explore the role, if any, of mGlu5 and mGlu7, which are highly expressed in most brain areas, on wakefulness and sleep in the rat.

Methods. 64 adult male Wistar rats (32 animals for each study) were stereotaxically prepared for polysomnography. Under general anaesthesia the animals were implanted with stainless steel electrodes screwed into the skull over the frontoparietal and occipital cortex for recording electroencephalographic activity. Two stainless-steel curved needles were inserted and fastened into the dorsal neck muscles for recording electromyographic activity. In the first study, 2-methyl-6-(phenylethynyl)-pyridine (MPEP), a selective glutamate mGlu5 receptor antagonist (5, 10 and 20 mg/kg, i.p.) or vehicle (physiological saline) were administered at the beginning of the light period. In the second study the effects on sleep of N,N'-dibenzyhydryl-ethane-1,2-diamine dihydrochloride (AMN082), an allosteric positive modulator of presynaptic mGluR7 activity (5, 10 and 20 mg/kg, i.p.), were studied. Three hours of polygraphic recordings were evaluated for stages of vigilance. Four categories of sleep–wake states based on the wave form were considered: (a) wakefulness (W), (b) light SWS, (c) deep SWS, and (d) REMS.

Results. In the first study, as compared to the control group, MPEP showed dose-dependent effects upon sleep: decreased duration and number of REMS episodes and decreased latency for light and deep SWS. In the second study, results showed significant effects of AMN082 as compared with the control group: (a) increased duration of light SWS with 5 and 10 mg/kg, whereas with the higher dose (20 mg/kg) a decreased duration of light SWS was observed; (b) decreased duration of W (5 and 10 mg/kg), with an increased duration of W in animals treated with 20 mg/kg; and (c) all doses decreased total duration of REMS.

Conclusion. These findings suggest a possible role for glutamate mGlu5 and mGlu7 receptors in the regulation of wake and sleep that needs to be further studied.

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Frequency and topography specific EEG activation during NREM and REM sleep prior to dream recall

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Objectives. Dreaming is not an exclusive domain of REM sleep, as evidence supports NREM dreaming, although the underlying motif remains uncertain. Here we investigated the EEG power density during NREM and REM sleep associated with and without dream recall.

Methods. NREM and REM sleep EEG activity with and without dream recall was analyzed in 17 young subjects (20–31 years) during a 40-hour multiple nap protocol (150 minutes of wakefulness and 75 minutes of sleep; 10 naps at total) under constant routine conditions.

Results. During NREM sleep, a significant interaction between factors ‘derivation’ and ‘recall’ was elicited in delta (1-3Hz) and sigma (12-15.5Hz) ranges ($p<0.05$). With respect to topographical differences, NREM sleep was associated with lower EEG power density for dream recall in the delta range, particularly in frontal derivations, and in the sigma range in centro-parietal derivations. During REM sleep, a significant interaction between factors ‘derivation’ and ‘recall’ occurred in alpha (10-12Hz) and beta (14-19Hz) ranges ($p<0.05$). Topographical analyses revealed that dream recall was associated with low frontal alpha activity and with high alpha and beta activity in occipital derivations.

Conclusions. Our data indicate that dream recall occurs *in a continuum* after both NREM and REM sleep awakening, and that differences between recall and no recall are directly coupled to EEG frequency-specific changes during both sleep states. This dual NREM-REM sleep modulation may hold implications for the mechanistic understanding of dreaming.

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Evidence that neurons of the sublaterodorsal tegmental nucleus triggering paradoxical (REM) sleep are glutamatergic

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Introduction. Paradoxical sleep (PS), during which dreams occur, is a state characterized by cortical activation, rapid eye movements and muscle atonia. In the recent years, we attempted to identify the neuronal network responsible for its genesis using functional neuroanatomy, local pharmacology and unit recordings. We demonstrated that GABAergic neurons located in the periaqueductal gray and medullary reticular nuclei play a pivotal role in that network (Sapin et al., 2009; Boissard et al., 2002, 2003). We further showed that neurons triggering PS localized in the sublaterodorsal tegmental nucleus (SLD) are neither cholinergic nor GABAergic (Verret et al., 2005; Sapin et al., 2009). We hypothesized that these neurons are glutamatergic.

Methods. To test this hypothesis, we combined immunohistochemical detection of Fos, a marker of neuronal activation, with non-radioactive *in situ* hybridization of vGLUT2 mRNA (vesicular glutamate transporter 2) in control rats, rats deprived of PS for 72h with the inverted flower pot method and rats allowed to recover after such deprivation.

Results. We found out that a large majority of the Fos-labeled neurons located in the SLD in rats displaying a strong rebound of PS express the vGLUT2 mRNA. These results strongly suggest that the vast majority if not all of the PS-on neurons triggering PS located in the SLD are glutamatergic. Additional experiments are ongoing to provide a more detailed analysis of the results as well as the locations in other brainstem structures of glutamatergic neurons implicated in PS genesis.

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Experience-dependent structural and functional plasticity of auditory-motor systems in the human brain

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The adult brain is constantly changing. Dynamic, reciprocal relationships exist between brain structure, brain function, and behaviour. These relationships are the basis of cognition, learning, and brain plasticity.

Neuroimaging techniques based on magnetic resonance imaging (MRI) have made it possible for us to non-invasively probe the structural and functional differences between groups of people differing in diverse perceptual and cognitive abilities. However, several major limitations preclude a comprehensive view of how the brain changes in response to experience. First, most studies have examined a single structural or functional variable (e.g. grey matter volume using voxel-based morphometry). The result is an incomplete picture of how changes reported with different techniques relate to one another. Second, only a handful of studies have examined the effects of behavioural training over time, rather than differences between behaviourally distinct groups. This means the relative influence of pre-existing structural differences and training-induced changes cannot be deduced. Finally, most studies use specific laboratory tasks designed to isolate 'basic' brain functions or systems. Consequently, not much is known about how training on complex tasks affects the brain.

The aim of my research is to develop a more complete understanding about how behavioural experience affects brain structure and function in adults. To do this, I will focus on musical perception and production, which have been identified as a particularly good model system to understand these interactions because they involve complex, precise movements to produce organized sequences of sound. An MRI scan sequence will be used to collect data for several analyses in a single session; grey and white matter volume, cortical thickness, white matter track integrity, and white matter myelination. The scan sequence will be repeated after several months' training on either a challenging rhythmic or melodic task, and again following an additional period without training. The data will be used to investigate the nature and transience of structural effects of the training. Patterns of activity during task performance (as measured by BOLD fMRI) will also be acquired pre- and post-training. Structural and functional changes will then be correlated with performance measures.

The results of this research will contribute towards clarifying and specifying the nature of anatomical change with experience and its relationship to behaviour. In the future, this line of research will have implications for rehabilitation following brain trauma, with interesting ramifications for diagnostic applications, and for education and developmental interventions.

Intracranial evidence for human hippocampus involvement in motor sequence learning

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A large variety of daily life activities are organized into sequences of movements, whose improved execution depends on practice. It has been shown that sequential motor performance may continue to develop over time after practice has ended, particularly during sleep, suggesting that skill learning undergoes an off-line process of consolidation.
In our study we aimed to investigate the neural correlates of sleep-related consolidation following learning of a deterministic sequence of finger movements.
Continuous intracranial EEG (iEEG) data were acquired across wakefulness and sleep in two drug-resistant epileptic patients with implanted electrodes covering several brain areas. Patients performed the task during two sessions, one before (training session) and one after (test session) an experimental night of sleep. Additional random sequences were used in both sessions to evaluate sequence-specific learning. For each subject, polysomnographic data of the experimental night and of one baseline night were recorded, to assess sleep architecture.
To test the hypothesis that learning occurred only in relation to the structured sequence, we implemented a single-trial classification algorithm that can capture learning-dependent changes in iEEG signal related to single events. We then assessed the contribution of each measurement site to the classification accuracy, by using the same statistical algorithm, but dropping in turn each of the recorded area and re-evaluating the corresponding classification performance.

Our results showed that the classifier correctly assigned single iEEG trials from the structured sequence as belonging to either the initial training session or to the later test session, whereas it failed to do so for trials belonging to the random condition. While the random sequence involved a widespread brain network, the learning of the structured sequence selectively involved the hippocampus in both subjects. Consistently, an average event-related potential analysis performed on the same hippocampal sites suggested amplitude modulation as a function of learning phase, selectively for the structured sequence.
These findings provide, for the first time to our knowledge, electrophysiological evidence, with accurate temporal and spatial resolution, for the role of human hippocampus in learning-related changes in the neural representation of single events within sequentially-organized knowledge.

Cholinergic mediation of enhanced REM sleep in conditional CRH-overexpressing mice

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Objectives. Impaired sleep is a morbid symptom that often associates with depression. Especially, reduced slow-wave sleep and disinhibition of rapid eye movement (REM) sleep are characteristic in those patients. Recently, we demonstrated upregulated REM sleep in two types of different conditional CRH-overexpressing mouse models, *i.e.,* CNS-specific (CRH-COE-Nes) and forebrain-specific (CRH-COE-Cam). The results suggest that overexpressed CRH in the forebrain including limbic structures contributes to enhanced REM sleep, which may apply similarly to the case of depressed patients. The present study dealt with a mechanism of how our CRH-COE mice have driven more REM sleep, examining a possible involvement of altered cholinergic activity in REM sleep regulation.

Methods. Male CRH-COE-Nes mice implanted with EEG/EMG recording electrodes were used to test muscarinic receptor antagonist atropine. After baseline recording, the mice were subjected to 6-h sleep deprivation (SD) from the onset of the light period (ZT 0) and received atropine (2 or 6 mg/kg ip) at ZT 6. Recover sleep was compared between control and homozygous CRH-COE-Nes mice. In another experiment using CRH-COE-Cam mice, extracellular levels of acethylcholine (ACh) in the central nucleus of amygdala (CeA) were determined across a day by *in vivo* microdialysis.

Results. During baseline, homozygous CRH-COE-Nes mice showed constantly increased REM sleep, whereas after SD elevated levels of REM sleep became more evident compared with control mice. Atropine at both low and high doses similarly reduced REM sleep in control mice, but in homozygous animals REM sleep suppression occurred in a dose-dependent manner. The basal release of ACh in the CeA showed a circadian variation; during the dark period when animals were mostly active, the ACh levels were high. However, if compared with controls, homozygous CRH-COE-Cam mice showed constantly elevated ACh levels throughout 24 h.

Conclusion. Atropine exerted its effects on sleep in a larger extent in homozygous than in control CRH-COE mice. This suggests that cholinergic activity is higher in homozygous mice, which is also supported by our microdialysis results. In this model, overexpressed CRH in the amygdala may contribute to intensifying the cholinergic system, resulting in a long-term enhancement of REM sleep. As seen in depressed patients, CRH-COE mice would possess hyper-cholinergic sensitivity.

Relationship between inflammatory markers and sleep efficiency in kidney transplanted patients

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Background. Poor sleep quality is frequent among patients with end stage renal disease (ESRD). There is large amount of data about that cytokines might be involved in sleep regulation. Partial sleep deprivation can induce increases in circulating levels of pro-inflammatory markers (e.g. Interleukin-6 (IL-6) or Tumour Necrosis Factor-alpha (TNF-alpha)) but experimental evidence suggests that TNF-alpha can also increase sleep quantity. Chronic inflammation with elevated levels of pro-inflammatory cytokines is frequent among ESRD patients. However, very little is known about the association between inflammation and sleep in patients after kidney transplantation (Tx). Therefore in this analysis we aimed to examine the relationship between inflammatory markers (IL-6 and TNF-alpha) and sleep efficiency (SE) in Tx patients.

Methods. 100 randomly selected, stable, adult Tx patients participated in the study. All patients underwent a one-night complete polysomnography in a sleep laboratory. We collected details about medical history, medication, co-morbidities and socio-demographic characteristics. Laboratory measurements were also carried out for each patient.

Results. The mean (standard deviation; SD) age of the sample was 51(13) years, 57% were males, the median (interquartile range; IQR) SE was 80(13)%. The median (IQR) levels of pro-inflammatory cytokines were 2.0(2.0) pg/ml for IL-6 and 1.9(1.3) pg/ml for TNF-alpha. SE showed a significant negative correlation with age (Spearman's rho=-0.439; $p<0.001$) and IL-6 (rho=-0.337; $p=0.001$), and a marginally significant positive correlation with TNF-alpha (rho=0.198; $p=0.053$). There was no significant correlation between SE and markers of kidney function, and severity of sleep disorders (OSAS and PLMS). In a multivariate linear regression model IL-6 level was not associated with SE when controlled for age and sex in the total sample. However, in gender-stratified groups IL-6 was in a significant negative relationship with SE in males, but not in females, and TNF-alpha was positively and nearly significantly associated with SE in females, but not in males.

Conclusion. We found an independent, negative association of SE with IL-6 level among male patients, and a trend-like positive association with TNF-alpha in female patients. Further studies are needed to determine the direction of these relationships and the role of the robust gender differences.

Disruption of Sleep by Sound is Predicted by Spindle Density in Humans

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Introduction. Illuminating the conditions under which sounds can disturb sleep—and who is most vulnerable to them—is critical to protecting healthful sleep. This implies the identification of potential predictors for individual sensitivity to noise during sleep.
Given that the neural processing of sound during sleep is thought to be modulated by spindles, we thus hypothesized that a sleeping brain's rate of spindle production signals its unique sensitivity to sound.

Methods. Twelve healthy human volunteers (mean age 26.3 ±7.5[SD]) were studied in the laboratory for three consecutive nights, during which sleep was monitored with a full polysomnographic battery.
The first night was a quiet night, during which no sound was presented. The second and third nights were noisy nights: fourteen common sounds, each 10 seconds in duration, were presented to the sleeping participant. Sounds were initiated at 40 dB and presented every minute in 5 dB increments until an arousal was observed on the electroencephalogram (EEG). Sound intensities at which an arousal occurred were averaged across sound types during stage 2 sleep in order to obtain a single (mean) arousal threshold per individual.
Sleep spindles were detected during stage 2 sleep of the quiet night using an automatic algorithm applied to central EEG channels (C3, C4). The density of spindles was computed as the number of spindles per minute.

Results. We found that spindle densities on the quiet night were positively correlated with arousal thresholds during the two noisy nights ($r = 0.77$; $p = 0.003$).

Conclusion. These results demonstrate that it is possible to predict an individual's ability to maintain sleep in the face of external sound. Those with more abundant spindles are more resistant to sounds during sleep. Therefore an assessment of the sleeping brain's spontaneous activity, as reflected by spindle density, can serve as a biological marker for predicting individual resistance to acoustic stimulation during sleep. This finding might aide physicians in the care of patients by anticipating who is vulnerable to sounds and implementing strategies to mitigate them. This finding might also serve as a launching point for experiments looking to enhance the biological properties of the brain—with drug or device—that render it more resilient to noise-induced disruption.

Sleep Patterns in Hallucinating Parkinson's Disease Patients and in high-Prone Normal Individuals

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A continuum hypothesis states that visual hallucinations (VHs) lie on a continuum ranging from mild expressions in the normal population to vivid VHs in the clinical population (Crow, 1998; Slade & Bentall, 1988) with similar underlying aberrant functioning expressed across different cognitive domains. To test the applicability of the continuum hypothesis in the sleep domain, the results of healthy young participants (11 high-prone and 11 low-prone to VHs) and Parkinson's Disease (PD) patients (12 with and 16 without VHs) have been compared using actigraphy, sleep diary and questionnaires measures (the Epworth Sleepiness Scale, Johns, 1991; the Berlin Sleep Apnoea Questionnaire, Netzer, Stoohs, Netzer, Clark, & Strohl, 1999 and the Pittsburgh Sleep Quality Index, Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Strikingly similar arousal disturbances occurred in high-prone normal participants and PD patients with VHs, namely more disrupted night-time sleep patterns (PSQI factor 5), a higher chance of sleep apnoea symptoms, a lower satisfaction with sleep, more disturbed daytime sleep patterns (the PSQI factor 7), fragmented sleep with decreased sleep minutes, several awakenings and longer wake episodes during night time. The results suggest that it is not sleep related brainstem areas in general, but rather specific thalamic arousal dysfunction that are implicated in both VHs in PD and hallucination-proneness in the normal population. The results are linked to the studies from other clinical disorders. Further actigraphy studies investigating the role of sleep latency, and neuroimaging studies investigating the role of thalamus, are warranted to provide evidence for the involvement of the arousal components in the occurrence of VHs in PD and hallucination-proneness in the normal population. Finally, the importance of good sleep hygiene is discussed as a mean of successfully ceasing VHs.

REM and NREM sleep contributions in post-training consolidation of Declarative memory. An investigation in narcolepsy and idiopathic hypersomnia

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Objectives. Although a relative consensus exists about the contribution of post-learning sleep in the consolidation of novel information in long term memory, the definition of the respective contributions of sleep stages in memory consolidation processes remains a matter of debates. Scrima (1982) proposed the hypothesis that Slow Waves Sleep (SWS) contributes preventing retroactive interference on recently acquired information, whereas Rapid Eyes Movement sleep (REM) contributes consolidating this information.

Methods. In order to test this hypothesis, we studied post-learning consolidation and protection against interference processes in patients suffering from narcolepsy (n = 3) and idiopathic hypersomnia (n = 2), reputedly characterised by an excessive proportion of REM and SWS sleep respectively, and healthy volunteers (n = 10). After learning a list of unrelated word pairs (A) and a night of sleep under polysomnographic control, recall performance was tested in the morning under either control or interference conditions, spaced a few days apart. In the interference but not in the control condition, a novel list of word pairs (B) was learned just before delayed recall of the list A. List B was composed of word pairs in which the initial word of the pair was also presented in learned list A, hence creating interference.

Results. Polysomnographic analyses failed to confirm an excess of REM in narcoleptics, nor an excess of SWS in idiopathic hypersomniacs, whose medication was not modified for the study. However, behavioural data suggest memory consolidation deficits in subjects with a REM sleep proportion below the norms. Interference effects were not found in any population, suggesting a ceiling effect in performance.

Conclusion. To sum up, our preliminary data suggest a possible link between REM sleep and consolidation for verbal learning in declarative memory, adding elements to the existing debate in the literature. Further studies are needed to investigate the role of sleep stages in the development of resistance to interference during memory consolidation processes.

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Keywords: Sleep, Memory, Hypersomnia

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Dissociable consequences of memory reactivation during sleep and wakefulness

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Objectives. According to the reconsolidation theory, reactivation during wakefulness transiently destabilizes memories and renders them susceptible to interference. Here, we tested whether the same basic principle applies to memory reactivation during sleep.

Methods. We reactivated memories by associated odor cues either during slow wave sleep (SWS) or during wakefulness, and reactivation was immediately followed by an interference task.

Results. As expected during waking, reactivation destabilized memories such that these memories became disrupted by interference learning. In contrast during SWS, reactivation stabilized memories and made them resistant to interference. In support of these behavioral findings, functional magnetic resonance imaging revealed strong differences in reactivation-induced brain activity between sleep and wakefulness. Reactivation during SWS mainly activated hippocampal regions and the retrosplenial cortex, whereas during wakefulness reactivation was primarily associated with activations in prefrontal areas.

Conclusion. Our results suggest that memory reactivation during SWS and wakefulness are functionally distinct processes.

Social effects on circadian behavior in ant

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Objectives. Circadian rhythms are present in almost all organisms. Light is thought to be the major cue that entrains the circadian clock and, thus, the rhythm of locomotor activity. Almost all experiments in the circadian field have been performed in isolated individuals and have ignored the effect of the social context on circadian behavior.
Eusocial insect species like ants are characterized by a division of labor: a large array of tasks has to be performed by the individuals, some of them requiring around-the clock activity like nursing, some others rhythmic activity like foraging. They represent a suitable model to study the influence of social context on the circadian clock and its output rhythms.
The aim of our study is to address the effect of social context on circadian rhythms in an ant species and to characterize at the molecular level its circadian clock.

Methods. Our ant model is Camponotus fellah. To follow the locomotor activity of all individuals we developed a tracking system with code bars glued on the back of each individual. The colony is placed under a high-resolution camera that takes 2 pictures/sec. The coordinates of each tag are extracted from each frame and the activity level is determined by comparing the position on two successive frames. The entire colony is kept under 12h Light and 12h Dark (LD) cycle or constant darkness (DD) with humidity and temperature controlled. The core clock genes were sequenced and their expression pattern studied under different social conditions.

Results. Most of the ants are arrhythmic inside the colony with a burst of activity at light-dark transition. Under both LD and DD, there was strong activity rhythm when ants were isolated. Interestingly, this rhythm mostly disappears when ants were with nestmates into the colony. The clear circadian rhythm of isolated ants seems to be driven by the circadian clock as the rhythm free runs (with a period of less that 24h) under DD conditions. Clock gene expression under arrhythmic (social) and rhythmic (isolation) condition is under investigation.

Conclusion. Our results suggest that social context is a major determinant of behavioral circadian rhythms.

REM sleep increase after acute deep brain stimulation of the subgenual cingulate gyrus in patients with treatment resistant depression.

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Treatment resistant depression (TRD) is a disabling and chronic illness, a core symptom of which is severe sleep disturbance. Deep brain stimulation (DBS), has been used in about 50,000 patients with Parkinson's disease worldwide and is now investigated as a treatment option for patients with TRD. Approximately 100 TRD patients worldwide are now receiving DBS, in different anatomical targets. Early results suggested that DBS alters subjective sleep in TRD patients (Mayberg 2005; Lozano 2008). To our knowledge we are the only centre reporting objective sleep changes as measured by polysomnography.

Electrodes are implanted bilaterally in the subgenual cingulate (SGC) and ventral anterior capsule nucleus accumbens (VACNAc). Patients are randomised to receive continuous bilateral stimulation in one of the areas alone for a period of at least 4 months after which stimulation can be switched to the second target. Overnight polysomnographic recordings were carried out at regular intervals before and during DBS treatment. Here we report on the whole sample at baseline (n=8) and on the four patients who received SGC stimulation first.

REM sleep suppression was a feature of most patients' sleep at baseline, reflecting their antidepressant medication (Wilson 2005) although 2 patients (1 trazodone, 1 trimipramine) exhibited no REM suppression. Those patients receiving SGC stimulation first (n=4) all displayed REM suppression at baseline and had a consistent increase in average REM sleep time (from 22min at baseline to 117min) and shortening of REM latency (from 209min to 114min) during recording in the first week after stimulation was commenced. These values returned to baseline levels with chronic stimulation (REM min 26; REM latency; 177). This change in REM was not apparent in those receiving VACNAc stimulation first.

Acute stimulation in SGC appears to increase REM sleep, which is lost during chronic stimulation, suggesting an adaptive mechanism. While DBS in Parkinson's disease has been reported to increase REM when stimulating the pedunculopontine nucleus which is germane to sleep physiology (Lim et al, 2009) so far no studies have documented the possibility of higher cortical areas such as SGC having an influence on REM sleep. SGC stimulation may exert its effects through connections to the hypothalamus or to lower brain stem nuclei involved in REM regulation, although this mechanism remains poorly understood.

Memory Consolidation During a Daytime Nap

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Objectives. The aim of the present nap study was to contribute to the heatedly discussed issue in sleep research whether the beneficial effects of sleep on the retention of information is due to active consolidation processes or simply due to the lack of interference during sleep. We studied the effects of naps during lunch time versus relaxation training, two relatively interference-free conditions, on the retention of face-word associations and single faces. We looked for a relationship between specific sleep stages/parameters and the performance gains over the nap.

Methods. Subjects incidentally learned face -written city pairs and single faces before a daytime nap or a relaxation training. Subjects retrieved half of the learning material before and half following the 90 min. study-test interval filled with sleep or relaxation. For retrieval, faces were presented alone for the cued recall of the associated cities. Single face retrieval was assessed with a recognition test. This protocol insured that pre-and post-tests measured effects of initial encoding and consolidation rather than re-encoding and re-consolidation. Four to seven months following the experiment, the retention of all learning material was re-assessed to investigate longterm effects of napping versus relaxing.

Results. For the cued recall, medium-performers (hit rate = .33, no ceiling performance) in the nap group showed less forgetting over the 90 min. delay than medium performers in the relaxation group. Subjects' face recognition performance in the nap group decreased less over the 90 min. delay than in the relaxation group. A median split revealed that only those subjects within the nap group with long SWS durations (> 17 min.) retained much of the learned single faces. Delta and fast sigma band power within the first 20 min. of sleep stage two was higher for those subjects who forgot fewer cities associated with a face over the nap. Total sleep duration did not correlate
with any of the pre-post memory score differences. Follow-up testing revealed better retention of face -written city associations reactivated before napping than reactivated before relaxation training.

Conclusion. Not only a night's sleep, but also a short nap may benefit the retention of learned material. Two aspects speak in favor of an active consolidation process engaged during sleep rather than a mere lack of interference: 1) Memory retention in the nap group was better than in the low-interference relaxation group, and 2) specific rather than global sleep stages/parameters are associated with better memory conservation. In long term, information reactivated before the nap was better retained than information reactivated before the relaxation training.

A short nap reverses leukocyte increase induced by an acute sleep restriction

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Short sleep duration during extensive work shifts is often experienced by workers such as intern and resident physicians while epidemiological data implicate poor sleep as a predictor of cardiovascular risk. Napping is a potential countermeasure to reverse fatigue but its effects on inflammatory markers are still unknown.

In a randomized crossover study with 2 periods and 2 conditions (nap, no-nap), we assessed the effects of a short nap on alertness and inflammatory blood parameters. Each subjects performed, one condition with a 30 min midday nap after the sleep restriction night (2 hours of sleep) and one condition without nap, under controlled conditions of caloric intake and continuous electroencephalogram monitoring. Nine young healthy men (mean age 22,2 years ± 2,33) were included in the study. Leukocyte counts and subsets (neutrophil, lymphocyte, monocyte), high sensitivity C-reactive protein, lipid profiles, maintenance of wakefulness test, Stanford sleepiness scale and sleep electroencephalogram recordings were performed.

We found increased leukocyte and neutrophil counts after sleep restriction that persisted after the recovery night in the no-nap condition but were reversed in the nap condition. After napping, the rebound of slow-wave sleep observed during the recovery night in no-nap condition disappeared and objective and subjective sleepiness was reduced. Our results indicate that after an acute sleep restriction, a short nap can decrease fatigue but also leukocyte count, a clinical marker of inflammation and strong predictor of cardiovascular mortality.

Inter-hemispheric spectral coherence reduction in sleep spindle frequency activity in patients with cognitive decline associated with aMCI and AD

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Objectives. There is ample evidence that progression of cognitive decline in Alzheimer's Disease (AD) is associated with a reduction in sleep spindle number, duration and amplitude as well as with altered spindle morphology. However, there is relative paucity of fast and objective methods to quantify such trends for potential diagnostic and prognostic purposes. Our objective is to identify easily derivable spindle-related parameters, quantitatively correlated with gradual cognitive decline from amnesic mild cognitive impairment (aMCI) to full-blown AD.

Methods. Sleep recordings, including 8 EEG channels (F3, F4, C3, C4, P3, P4, O1, O2), were performed on 4 patients with AD (3F, 1M; age: 73±5 years), 6 patients with aMCI (5F, 1M; age: 75±3 years) and 4 healthy controls (1F, 3M; age: 67±7 years). All patients were diagnosed via standard procedures and were drug-naïve. EEG traces of well-formed spindles from stage II in the first, middle and last third of the night sleep recording were visually selected and subjected to automated analysis for calculation of the following spindle parameters for each subject, as well as for each group of subjects: Spectral power (FFT squared) of channels C3 and C4 in the range 10-16 Hz, spectral center of gravity in these channels in the range 10-16 Hz, and mean spectral coherence between channels C3 and C4 in the range 10-15 Hz.

Results. Spectral coherence in healthy controls varied within the range 0.56 - 0.74 (mean 0.65), in aMCI patients within the range 0.37 - 0.59 (mean 0.47), and in AD patients within the range 0.26 - 0.54 (mean 0.40). Statistical comparison (Wilcoxon rank test) showed significant differences between controls–aMCI ($p=0.033$), and control-AD ($p=0.021$), and trend between aMCI-AD ($p=0.28$). No significant differences in spectral power or spectral center of gravity were detected.

Discussion. The results suggest that spectral coherence between channels C3 and C4 in the sleep spindle frequency band may be a sensitive marker associated with pathological cognitive decline and, in view of its relative ease of derivation, may prove clinically useful. This reduction in inter-hemispheric EEG synchrony may be related to the recent MRI evidence of thalamic involvement since the early stages of AD.

Multicenter study about agreement between CPAP titration by polisomnography and predictive formula in sahs patients

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Introduction. Miljeteig & Hofstein designed a predictive formula in 1993 in order to determine the initial CPAP pressure in SAHS Canadian patients and this method has been widely used for titrating CPAP, without previous scientific validation in our environment.

Objectives. Analyse the concordance between CPAP titration by polisomnography (gold-standard technique) and by the Miljeteig and Hofstein's predictive formula in a multicenter population.

Methods. 830 patients from 3 different hospitals from Region of Valencia , Spain (Doctor Peset University Hospital [HPV], Lluis Alcanyis Hospital [HLX] and Verge dels Lliris Hospital [HVA]) were analysed after a complete data collection. Agreement beyond chance between both methods was judged by Lin's coefficient (Rho)

Results. The average CPAP titration by polisomnography ranges from 7.4 (HVA) to 10.9 (HLX) cm H_20. We found a slight agreement in HPV (Rho= 0.102 IC95% -0.13 a 0.33) and HLX (Rho= 0.19 IC95% 0.14 a 0.24) and moderate in HVA (Rho= 0.45 IC95% 0.32 a 0.59).

Conclusion. The Miljeteig & Hofstein's predictive formula does not show a good concordance in our sample. According to these results, we rather recommend CPAP titration by polisomnography in SAHS patients until more studies would be able to prove if there is another alternative method of titration with enough scientific evidence to replace the polisomnography.

Influence of passive changes of bed climate on sleep quality

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For the quality of sleep several physiological processes including thermoregulation are important. Core body temperature is related to restful sleep. Most of the studies in this field investigated thermoregulatory aspects in relation to modulation of ambient temperature. The aim of this pilot study was to investigate the influence of passive changes in the bed climate (temperature and humidity in the space between mattress and blanket) on sleep of healthy subjects.

While external conditions where kept constant, two blankets with different temperature and moisture dissipation characteristics were used to create different bed climates. Blanket A was equipped with apertures to allow more dissipation of temperature and humidity, in all other respects it was identical to blanket B. In a standardised, randomised and double-blind cross-over design 12 test subjects underwent three consecutive nights of polysomnography. The first night was a habituation night, in night 2 and 3 they used either of both blankets. Temperature and humidity in the test room and bed climate was measured in six of the 12 subjects.

Results show a tendency that with blanket A the bed climate is more cool and dry. Arousal index, sleep efficiency and total sleep time showed a slight but not significant improvement with blanket A. Finally this pilot study indicates a tendency towards improvement of sleep quality in association with a drier and cooler bed climate. These findings warrant further investigations with higher numbers of subjects to confirm this tendency.

Benefits of napping and an extended duration of recovery sleep on alertness and immune cells after acute sleep restriction

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The recovery process following sleep restriction has not been extensively studied with regard the immune and inflammatory systems and sleepiness.

We studied healthy young men during a 2-hr sleep-restricted night followed by either a normal 8-hr night of recovery sleep (n=12), a 30-min midday nap plus an 8-hr recovery night (n=10), or a 10-hr extended recovery night (n=9). Subjects underwent continuous electroencephalogram monitoring. A control group of healthy young men slept for 3 consecutive 8-hr nights (n=9). Blood leukocytes and subsets, inflammatory and atherogenesis biomarkers (C-reactive protein, interleukin-8, myeloperoxidase, fibrinogen and apolipoproteins ApoB/ApoA), sleep patterns and sleepiness were investigated.

All parameters remained unchanged in the control group throughout the study. After sleep restriction, leukocyte counts were increased, an effect that persisted after the 8-hr recovery sleep, but, in subjects who had a nap or a 10-hr recovery sleep, these values returned nearly to baseline. The lymphocyte count was reduced after normal but not after extended recovery sleep. Inflammatory and atherogenesis biomarkers were unchanged except for higher myeloperoxidase levels after sleep restriction. Saliva cortisol decreased immediately after the nap. The rebound of slow-wave sleep observed during the 8-hr recovery night was not present in subjects who had had a nap. The increased sleepiness observed after sleep restriction returned to baseline only in the nap and extended sleep recovery conditions.

Our results indicate that modulating recovery sleep after sleep restriction by having a short nap or extending the duration of recovery sleep can improve alertness and return leukocyte counts to baseline values.

Differential electrodermal and phasic heart rate responses to personally relevant information: Comparing sleep and wakefulness

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Objectives. The aim of this study was to determine whether a differential physiological reaction to personally relevant information exists during sleep and if it is comparable to the reaction pattern observed during wakefulness.

Methods. Thirteen subjects (10 male and 3 female) slept in the sleep laboratory on two consecutive nights. During both nights a polysomnogramm was recorded, in the second night – the experimental night – electrodermal and heart rate reactions were recorded additionally. Sequences of 50 audio samples consisting of ten repetitions of each the subject's own first name and four other first names were played in a random order during sleep stage 2, rapid eye movement (REM) sleep and wakefulness.

Results. Across all conditions, larger skin conductance responses were elicited by subjects' own first name. During REM sleep, personally relevant information led to larger heart rate acceleration, whereas an enhanced deceleration was found during wakefulness.

Conclusion. These findings suggest that auditory information is processed on a semantic level even during sleep. However, personally relevant information elicits a co-activation of the sympathetic and the parasympathetic nervous system during the wake state while only the former system is activated during REM sleep. The response pattern in the wake state reflects a mechanism focusing attention to a specific stimulus source – termed the orienting response. In contrast, the physiological responses during sleep seem to be part of a different mechanism aiming to wake the subject after crucial information has been detected in the environment.

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Obstructive Sleep Apnea-Hypopnea Syndrome (OSAHS) diagnosis by human voice analysis. Preliminary Results.

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Most recent estimates indicate that around 2 million people suffer from OSAHS in Spain, but only 10% have been diagnosed. OSAHS diagnosis requires very long and expensive testing so it is necessary to develop faster and easier testing methods. The human voice is effected by superior airway physiology and anatomy, so its analysis can be usefull for OSAHS diagnosis. The aim of this study is to develop a new tool for OSAHS diagnosis using the voice.

It was a multicenter, prospective, randomized and blind study. Healthy people and patients with clinical suspicion of OSAHS underwent a polysomnograpy study (PSG), a voice recording and a medical evaluation. Their blood pressure and anthropometric measurements were taken and they answered questionnaires on health, sleepiness and sleep habits. First, the most relevant clinical variables of both groups (healthy and OSAHS patients) were determined by Classification and Decision trees, and voice spectral analysis was done. Second, a neural net was trained to discriminate healthy people (Apneas-Hipoapneas Index (AHI) < 10) from OSAHS patients (AHI > or = 10) by using the most relevant clinical variables and the spectral characteristics of voice.

Out of the 542 subjects on which PSG and voice recording were performed 337 of the voice recordings were evaluable. 252 voice characteristics and 7 clinical variables were analyzed. Final analysis were done with 7 voice characteristics and 3 clinical variables (sex, age and Body Mass Index). A correct classification rate (AHI < 10 or AHI > or = 10) was 82,7%. Interestingly, most of the false positives and false negatives were in border zones. Sensibility was 0,88 (95% Confidence Interval (CI) 0,78-0,98), specificity was 0,75 (95 CI 0,62-0,88), Positive Predictive Value 0,78 (95% CI 0,66-0,90), Negative Predictive Value 0,86 (95% CI 0,75-0,97).

These preliminary results suggest that voice analysis can be a helpful tool to diagnose patients with clinical suspicion of OSAHS, either to rule it out or to confirm it.

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Disregulation of prion protein expression alters REM sleep homeostasis in aged mice

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The prion protein (PrP) is a glycoprotein anchored to cell membranes and expressed in most cell types, including neurons and glia. Although mutations in this protein lead to severe neurodegenerative disorders associated with major sleep alterations (i.e. Fatal Familial Insomnia and Creutzfeldt-Jacob disease), little is known about PrP physiological functions. The disregulation of normal PrP expression does not affect sleep under baseline condition (BL) in both young and aged PrP knock-out (KO) mice and in aged transgenic mice over-expressing PrP at ~4 times the physiological level [Tg(WT)] (Tobler et al, Nature, 380: 639-642, 1996; Dossena et al, Neuron, 60: 598-609, 2008). However, after sleep deprivation (SD), young KO mice showed alterations in REM sleep (REMS) rebound (Tobler et al, 1996).
Objectives. As prion disease symptoms appear most often in patients aged 50+, we hypothesize that, in mice with altered PrP expression, alterations in REMS compensatory response to SD could become more evident with aging. To test this hypothesis we performed sleep deprivation (SD) in aged mice in which PrP expression was genetically altered.

Methods. Male mice (18 months and older) of three different strains were used:
- C57BL/6J, wild type (WT) mice as control strain (n=7)
- PrP KO mice (n=4)
- PrP Tg(WT) (n=10)

Animals were maintained under a 12h-12h light-dark cycle, on a constant temperature of 26±1℃. They were implanted with EEG and ECG electrodes. After recovery from surgery EEG, ECG and gross body activity were recorded for 24h during undisturbed BL. The following day, starting at light onset, a 6h SD was performed by gentle handling. Recordings continued under undisturbed conditions for the remaining 18h of the day to evaluate the response to sleep loss.

Results. During the first 6h following SD, a significant increase (49.20±11.6%) in REMS amount was observed in WT mice (BL: 6.3±0.5 vs SD: 9.3±0.9, % of recording time; t-test <.05), whereas no significant rebound in REMS was observed in KO and Tg(WT) mice. During the first half of the subsequent dark period, WT mice still showed a large increase (273.5±53.3%) in REMS amount (BL: 1.8±0.7 vs SD: 5.8±0.4, % of recording time; t-test <.01), whereas REMS expression was not different from BL in KO and Tg(WT) mice.

Conclusions. These data suggest that in aged mice a disregulation in PrP expression, no matter if the protein is absent or over-expressed, can induce an alteration in the homeostatic control mechanisms regulating REMS.

Polisomnographycs results in Chiari malformation I

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Introduction. The symptoms in Chiari malformation type I (CM-I) have more different presentations, and depends on certains components of malformation and its possible association with siringomielia or hydrocefalia. Headache, cervical ache, dizzyness, muscular weakness, craneal nerve alterations and ataxia are frequent symptoms, but few patients present sleep complaints like hypersomnia or insomnia.

Objectives. Study of sleep architecture, respiratory parameters and leg movements in a group of CM-I patients.

Methods. Thirty nine patients with CM-I (26 women) with middle age of 38 ± 13,5 years underwent a nocturnal polisomnography (PSG)

Results. Sleep architecture had minimal alterations and increase in stage 1 and arousal respect normal values. The respiratory parameters were normal in 13 patients. Twenty six patients presented a sleep disordered breathing with apnea-hipopnea index (AHI) higher than 5. The respiratory alterations were predominantly obstructive and during the supine position.
There was a significative positive correlation between the AHI and REM latency, stage 1 and arousal index, and negative correlation between AHI and low REM percentage and number of sleep cycles.
There wasn't a periodic leg movement index in pathological range in these patients.

Conclusion. Patients with CM-I had an increased prevalence of fragmented sleep and sleep disordered breathing. This alterations may not be reported by patients and can only be detected performing a sleep study.
This study had partial financial support (Beca FIS:PI07/0681)

Is the two hour recommended maximum driving time appropriate for both healthy older and treated obstructive sleep apnoea drivers?

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Objectives. The UK Department for Transport recommends taking a break from driving every 2 h. This study investigated: (i) if a 2 h drive time on a monotonous road is appropriate for OSA patients treated with CPAP, compared with healthy age matched controls, (ii) the impact of a night's sleep restriction (with CPAP) and (iii) what happens if these patients miss one nights' CPAP treatment.

Methods.19 healthy men aged 52–74 y (m= 66.2 y) and 19 OSA participants aged 50–75 y (m = 64.4 y) drove an interactive car simulator under monotonous motorway conditions for 2 h on two afternoons, in a counterbalanced design;
(1) following a normal night's sleep (8 h)
(2) following a restricted night's sleep (5 h), with normal CPAP use
(3) following a night without CPAP treatment. (n=11)
Lane drifting incidents, indicative of falling asleep, were recorded for up to 2 h depending on competence to continue driving.

Results. Normal sleep: Controls drove for an average of 95.9 min (sd 37 min) and treated OSA drivers for 89.6 min (sd 29 min) without incident. 63.2% of controls and 42.1% of OSA drivers successfully completed the drive without an incident.
Sleep restriction: 47.4% of controls and 26.3% OSA drivers finished without incident. Overall: controls drove for an average of 89.5 min (sd 39 min) and treated OSA drivers 65 min (sd 42 min) without incident.
The effect of condition was significant [$F(1,36) = 9.237$, $p<0.05$, $eta2 = 0.204$].
Stopping CPAP: 18.2% of drivers successfully completed the drive. Overall, participants drove for an average of 50.1 min (sd 38 min) without incident. The effect of condition was significant [$F(2) = 8.8$, $p<0.05$, $eta2 = 0.468$] .

Conclusion. 52.6% of all drivers were able to complete a 2 hour drive under monotonous conditions after a full night's sleep. Sleep restriction significantly affected both control and OSA drivers. We find evidence that treated OSA drivers are more impaired by sleep restriction than healthy control, as they were less able to sustain safely the 2h drive without incidents. OSA drivers should be aware that non-compliance with CPAP can significantly impair driving performance.
It may be appropriate to recommend older drivers take a break from driving every 90 minutes especially when undertaking a monotonous drive, as was the case here.

A non-invasive, high-throughput approach for the assessment of sleep in mice in response to pharmacological and environmental manipulation

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Objectives. Sleep is a highly complex behavioural state, and presently the identity and full spectrum of genes underlying its regulation remain poorly defined. The current 'gold standard' method for determining sleep in mammals involves the surgical implantation of electroencephalogram (EEG) electrodes; which is largely prohibitive in terms of high-throughput screening. Advances in rapid, non-invasive behavioural assays to evaluate sleep are therefore extremely valuable, particularly in the evaluation of novel pharmacological compounds but also to support whole-genome mutagenesis and quantitative trait loci analysis. Recent studies have considered immobility as a surrogate measure of sleep; however the extent to which these methods have been validated and incorporated into a viable automated system is limited.

Methods. Here we describe the validation of a method using commercially available video-tracking software to assess sleep in mice based on the automated detection of immobility. Male C57BL/6 mice implanted with EEG telemetry transmitters were housed in light-tight ventilated chambers and were simultaneously recorded using miniature infra-red video cameras linked to a digital recorder. Using automated digital video analysis we assessed 24 hour baseline sleep/wake behaviour but also pharmacologically-induced sleep in comparison with EEG-defined sleep. The method was further evaluated by determining the effect of pharmacological compounds and environmental changes in light/dark exposure on sleep/wake behaviour.

Results. This approach gave an extremely high agreement with simultaneous EEG-defined sleep across a 24 hour period, with an estimated bias of just +0.48 minutes (95% confidence interval +3.41, -4.37 minutes) per 1 hour period. We demonstrate the sensitivity of the method, whereby the effects of different doses of zolpidem (1-10mg/kg) on sleep could be distinguished, and conversely were able to detect the disruption of sleep induced by caffeine (15mg/kg) during the habitual sleep phase. Furthermore, we could identify sleep/wake changes in response to environmental manipulation of the light/dark cycle.

Conclusion. Collectively, we have developed a relatively inexpensive and highly accessible system that represents a powerful primary stage screening tool for the assessment of sleep in mice, simultaneously permitting the investigation of additional behavioural repertories related to sleep/wake behaviour.

Motor-behavior during rem sleep of narcoleptic with cataplexy patients: a systematic classification

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Objectives. Provide a detailed and systematic analysis of the number and type of motor event occurances during REM sleep in Narcoleptic/Cataplectic (N/C) patients through video-PSG analysis.

Methods. 17 patients with a clinical and video polysomnographic diagnosis of RBD underwent an experiment of video-PSG and a questionaire to evaluate RBD syntomatology. Based on the classification of motor events proposed by Frauscher et. all (2007), the motor events were classified as:1) Elementary: a) myoclonic events; b) simple events; 2) Complex: a) complex events; b) scenic events; c) aggressive and/or violent events; 3) Vocalization. All the parameters taken into account in this study was statistical analysed.

Results. From the results drawn from the questionnaire, 11 patients NC (Narcolepsy+RBD) had a clinical diagnosis of RBD and other 6 resulted RBD negative (Narcolepsy-RBD). Amoung the 325 motor events registered for the group of Narcolepsy-RBD patients, 283 were classified as elementary (140 myoclonic events; 143 simple), 34 complex (34 complex events) and 8 vocalizations. Out of the 898 motor events registered in the narcolepsy+RBD group of patients, 704 were classified as elementary (238 myoclonic events; 465 simple), 135 complex (93 complex events; 37 scenic events; 5 aggressive events) and 60 vocalizations. The scenic motor events were found in 4 (36.4%) of the patients with Narcolessia+RBD and only one patient showed aggressive behaviour (9%). These parameters are not statistically significant between the two groups.

Conclusion. This systematic analysis of motor activity during REM sleep of NC patients with and without clinic RBD allowed us to draw the conclusion that in the NC patients, the majority of motor events during sleep can be classified as elementary.
It can also be noticed that the frequency of very aggressive and violent behaviour, which belong to other secondary manifestations of RBD, were not found.

Reference
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The lowest desaturation in patients with sleep apnea syndrome is an independent factor for systemic hypertension

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Introduction. The patho-physiological hallmark of obstructive sleep apnea (OSA) is nocturnal intermittent hypoxia.

Aims and objectives. Analysis of oxygen desaturation variables and correlations with apnea – hypopnea index and systemic hypertension (SH).

Material and methods. 817 consecutive patients with suspected obstructive sleep apnea were evaluated with sleep questionnaires, anthropometric measurements, polisomnography for AHI (apnea-hypopnea index normal 0-4, mild 5-14, and moderate 15-29, severe over 30). We measured the Odds Ratio (OR) together with 95% confidence interval (CI) in an univariate analysis and the independent variables were used in order to identify the most important predictors. Multiple linear regression analysis was performed.

Results. 748 (91,55%) patients had OSA, 541 males (72,47%), 208 females (27,53%), age 52 ±11,89 years (16-84), AHI 34,10/h ± 27,41, 65,61% with systemic hypertension (SHT), 16,18% with COPD, lowest desaturation (LD) 70,49 ± 16,39 % (23-93), desaturation index (DI) 30,64 ± 24,30/h (6-128), medium desaturation (MD) 91,98 ±4,01%. The DI is not linear correlated with AHI and in multivariate analysis is an independent factor for OSA (OR 3,11, p< 0,001, 95% confidence interval 2,67-4,59). In multiple linear regression analysis the relationship between AHI and the DI is direct proportional and the corelation is powerful, r = 0,7465, p <0,001. DI was significantly higher with SHT (31,12/h vs 20,21/h, p < 0,001) and COPD (36,24/h vs 24,6/h, p = 0,004). The relationship between the AHI and MD is inversely proportional, r = 0,30, p<0,001 and values are significantly different in SHT (90,6% vs 92,93%, p < 0,001) and COPD (89,87% vs 91,89%, p < 0,001). LD is an independent factor for SHT (OR 3,78, p< 0,001, 95% confidence interval 2,89-4,87).

Conclusion. The desaturation index, medium desaturation and lowest desaturation are significantly lower in patients with OSA and co morbidities (systemic hypertension, COPD). The lowest desaturation is an independent factor for systemic hypertension.

Severity of diabetic control is positively correlated with an increased risk of having OSA

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Objective. To determine the impact of haemoglobin A1C (HbA1C) which is the most important marker of glyceamic control in type 2 diabetic patients on the risk having obstructive sleep apnea. The secondary aim is to determine if the correlation results are similar for both sexes.

Methods. 974 male and female patients with type 2 diabetes have been recruited from the diabetes clinic database at the local hospital between January and December 2009 and each patient's HbA1C was recorded. All patients have been given a questionnaire based on the Berlin validated questionnaire asking for daytime somnolence, snoring and apnoeas. Selected patients are being screened for the presence of obstructive sleep apnea by the overnight oximetry method.

Results. 61 % of the selected 974 patients answered the questionnaire of whom 56% were male and 44% female. Based on their submitted answers to the questionnaire, patients have been designated as either 'high risk' for OSA (66 %) and 'low risk' for OSA (34%). A 100 patients have been randomly selected for overnight oximetry tests which are currently being carried out. Preliminary results show a positive correlation ($r = 0.41$, $p = 0.003$) between the level of HbA1C and the number of >4% Sa_{O_2} dips/hour obtained from oximetry. Similar trends have been observed in both females and males.

Conclusion. Preliminary results show that severity of diabetic control is positively correlated with an increased risk of having OSA and furthermore no gender differences have been observed.

Sleep Does not Affect Binding Process in Episodic Memory

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Objective. Binding refers to the complex mechanisms by which distinctive information elements are linked together in episodic memory. We have tested whether post-training sleep affects binding processes after intentional or incidental learning.

Methods. Twenty participants underwent 3 experimental sessions across two days. The first session took place either in the morning or in the evening. Subjects had to learn a list of 60 words printed in different colors. They were instructed to retain the words for delayed testing, but were not informed that knowledge of the associated color will be also tested (incidental binding). In the second session, after 12 hours filled either with sleep (night) or wakefulness (day), they performed two recognition tests on (a) words alone (printed in black) and (b) words with their associated color. Subjects then learned a second list of 60 words printed in different colors. This time, they were instructed to remember both the word and the associated color (intentional binding). In the third session, after 12 hours of sleep or wakefulness, they had to recognize words from the second list, again in word-alone and word-color association conditions.Repeated measures ANOVAs with binding type (incidental vs intentional) and post-learning interval (sleep or wakefulness) factors were computed on recognition performance under the two conditions.

Results. Results disclosed that binding memory for words with colors was higher in the intentional than in the incidental condition ($p<.05$), suggesting that intentionality at encoding improves the efficiency of binding processes. A beneficial effect of post-training sleep on memory for words alone was found in the incidental binding condition only ($p < .05$).

Conclusion. Our results suggest a beneficial effect of post-training sleep on off-line memory consolidation for verbal material, in line with the existing literature. At variance, intentionality at encoding, but not post-training sleep, seems to favor binding processes in episodic memory.

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Sleep length, Television and Computer habits and Overweight in Swedish School - Aged Children and Adolescents

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Sleep problems impact on children's health, learning and school performance, quality of life, as well as on the family. The aim of the present descriptive cross-sectional study was to investigate sleep duration, television and computer habits, difficulties sleeping, feeling of tiredness in school, and overweight, and to study associations between television and computer habits and sleep problems. The questionnaire was constructed to be used at the health visits at the school health care in preschool class or at grade 1, and 4, 8 and 10 when the children are approximately 6 or 7, 10, 14 and 16 years respectively. During the school year of 2008-2009 the school nurses distributed the sleep questionnaire, and this resulted in 3021 answered questionnaires. The mean length of sleep per night was found to be 10 hours at the age of 6-7 years, 9 hours and 35 minutes at the age of 10 years, 8 hours and 5 minutes at the age of 14, and 7 hours and 30 minutes at the age of 16 years. The children were divided into two categories in terms of length of sleep: those sleeping less than median sleep length in their grade (short sleep) and those with longer sleep. Those sleeping less reported being tired in school more frequently (p=0.001), having difficulties falling asleep (p=0.001), difficulties waking up (p=0.001), having a bedroom TV (p=0.001), spending 2 hours or more at the TV (p=0.001) or computer (p=0.001).

Key words: Sleep length, Television, Computer, Overweight, School - Aged Children, Adolescents

Contribution of adenosine related genes to the risk of depression with disturbed sleep

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Objectives. Most patients with major depression report problems in their sleep: insomnia, early morning awakenings and fatigue correlating with poor sleep quality. One of the key substances regulating sleep is adenosine. We hypothesized that variations in polymorphic sites of adenosine related genes may predispose to depression with sleep disturbances.

Methods. We selected 117 single nucleotide polymorphisms from 13 genes and analyzed their association with depression and specific sleep problems (early morning awakenings and fatigue). Data were collected as part of the Health 2000 Study based on Finnish population and included 1423 adult subjects.

Results. Our major finding herein was, among women, the association of *SLC29A3* polymorphism rs12256138 with depressive disorder ($p=0.0004$, odds ratio=0.68, 95% CI 0.55-0.84, $p<0.05$ after Bonferonni correction for multiple testing). Only one gene showing any evidence for association was common to women and men (*ADA*).

Conclusions. Our results suggest that compromised adenosine transport due to variation in nucleoside transporter gene *SLC29A3* in women, could predispose to depression, and could suggest new directions in treatment research. The shortage of overlapping genes between the genders indicates that the genetics of mood regulation may vary between the sexes.

Centre of Reference for Rare Hypersomnias, a great opportunity for physicians and patients

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Objectives. Thanks to the French National Plan for Rare Diseases of the Ministries of Health and of Research 2005-2008, the Sleep and Vigilance Centre of Hotel-Dieu (Paris, France), has been labeled Centre of Reference for Rare Hypersomnias in October 2005. One focus and priority of the Centre is developing information and help for patients, health professionals and general public concerning hypersomnias and narcolepsy.

Methods & Results. In that perspective, we developed different tools. We started in 2006 with the realisation of the “Emergency Healthcare Card” for narcoleptic patients in collaboration with the French Ministry of Health. In order to improve care and epidemiological data, we put in place a shared medical history for hypersomniac patients. In parallel, we designed a website “www.je.dors.trop.fr” devoted to hypersomnias to help with administrative processes for educational or professional integration and to give advices for everyday life (in family, at school or at work, with the doctor...). To complete this website, six more specific leaflets have been written: “Narcolepsy and women”, “Narcolepsy and occupational guidance”, “Tools of screening and follow-up care for Narcolepsy”, “Narcolepsy and nutrition”, “Narcolepsy and other sleep troubles”, “Nap and rest in Narcolepsy”. Finally, to promote exchanges between physicians and patients, we organize every year since three years the “Workshops of Narcolepsy”. These are one-day practical workshops dedicated to the patients and their family, with the participation of specialists, on various themes linked to hypersomnias and narcolepsy.

Conclusion. Every year, we sound out patients about their expectations to go on improving care and knowledge on hypersomnias. Till now, their comments are very positive to continue. In 2008, we also performed an auto-evaluation from the Ministries of Health and of Research. Their feedback was encouraging and we hope that the next assessment at the end of this year will be as good.

Interrelationship between baseline sleep architecture, circadian activity pattern and cognitive deterioration in the APP23 mouse model of Alzheimer's disease

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Objectives. Sleep and circadian rhythm disturbances frequently occur in patients with Alzheimer's disease (AD) and disruption of sleep-wake patterns parallel the characteristic decline of cognitive abilities, even within the mildest forms of AD. Evidence supporting their correlation is growing and even points out a possible predictive value of disturbances in sleep continuity and architecture regarding AD-related cognitive deterioration.
In accordance with clinical AD, the well-validated APP23 transgenic amyloidosis mouse model of AD displays an age-dependent decline in visuo-spatial learning abilities, fist appreciable at the age of 3 months, preceding A-beta plaque deposition and disturbances in horizontal locomotor activity reminiscent to sundowning. This study aims to establish whether 3-month-old APP23 mice display disruptions in baseline sleep architecture and circadian activity profile in comparison with age- and gender-matched wild type control littermates. Furthermore, if alterations in circadian sleep-wake and/or activity patterns in accordance with clinical AD are present, we will further elucidate whether or not these changes coincide with decline of spatial memory capacities as previously observed within this mouse model of AD.

Methods. Male, heterozygous APP23 mice (n=8) and their age- and gender-matched wild type control littermates (n=8) are surgically implanted with epidural electroencephalographic electrodes over the frontal and parietal cortex, a reference electrode above the cerebellum and two nuchal electromyographic electrodes to enable electrophysiological recording of sleep. Following a one-week recovery period mice are allowed to habituate to recording conditions for 5 consecutive days after which EEG/EMG and home cage-activity are simultaneously recorded at the age of 12 weeks to generate 24 hour baseline patterns of sleep-wake architecture and horizontal locomotor activity in a 12h/12h light-dark cycle. One week post-recording the mice are subjected to a hidden-platform Morris-type water maze training protocol consisting of eight trial blocks, followed by a probe trial with removal of the platform to assess spatial learning and memory.

Results & Conclusion. Preliminary data will be presented, adding to the further validation of the APP23 mouse model of AD and a better understanding of the interrelationship between sleep changes, circadian rhythm disturbances and cognitive deterioration in AD.

Memory Consolidation of a New Task is inhibited in Ethiopian Psychiatric Patients

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Objectives. Schizophrenic and depressive patients show impeded sleep dependent procedural memory consolidation. But this has been shown mainly for tasks testing the adaptation of old skills. This study tested the overnight memory consolidation of a new task and the transfer of this new skill to a similar task.

Methods. Using an adapted version of the sequential finger tapping task, keyboard-naïve Ethiopian depressive (n=8) and schizophrenic (n=15) patients and healthy controls (n=11 and n=17) were tested twice, 24 hours apart. In addition the subjects underwent training in a second sequence after the retest of the first sequence.

Results. Both schizophrenic and depressive patients did not show a significant overnight change in performance (1% and 4% improvement respectively) in the task and differed significantly from the healthy control groups who did show significant improvement (16% and 22%). Further in contrast to the healthy controls both patients groups showed no significant transfer of the newly acquired skill to the second sequence.

Conclusion. This study shows that depressive and schizophrenic patients are not only deficient in the overnight memory consolidation of a new task, but also fail to show a transfer of this new skill to similar tasks.

The influence of amitriptyline on visual perceptual learning in healthy subjects

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Numerous studies provide evidence that rapid eye movement (REM) sleep is important for consolidating perceptual skill memory, whereas the consolidation of motor skill and declarative memories is thought to be linked to stage 2 or slow wave sleep. Therefore, pharmacological REM sleep suppression by amitriptyline may impair improvement in perceptual skill memory in contrast to motor skill or declarative memory.

Thirty-two healthy males participated in the double blind, placebo controlled, randomized, parallel design eleven-day study. Participants were instructed to maintain regular sleep schedules as controlled by actigraphy. During night nine and ten polysomnography was performed in the lab. Both evenings visual discrimination task (VDT), finger sequence tapping task, Rey Auditory-Verbal Learning Test and Rey-Osterrieth Complex Figure Test were performed. In night ten participants received at 9:30 pm and 1:30 am either two times placebo or amitriptyline with 25 mg at 9:30 pm and 50 mg at 1:30 am. One subject was excluded due to technical reasons. Because good quality sleep is a prerequisite for sleep associated learning, reported results were restricted to 24 subjects (amitriptyline: n = 12, placebo: n = 12) who rated their sleep as at least moderate restorative in the morning protocol after the investigation night.

Amitriptyline increased REM-sleep latency (amitriptyline: 197.25 +/- 107.24 min, placebo: 93.42 +/- 36.50 min) and reduced REM-sleep percentage (amitriptyline: 4.11 +/- 3.68 %, placebo: 19.40 +/- 5.23 %) while stage 2, total sleep time (TST) and sleep efficiency significantly increased and time spent awake significantly decreased as compared to placebo. Regarding memory tasks, compared to baseline condition VDT after investigation provides a significant group difference with impaired values in the amitriptyline group (-6.33 +/- 17.17 ms), but improved learning in the placebo group (7.08 +/- 12.59 ms). Furthermore, delta VDT correlates to TST within the amitriptyline group only.
Posttraining pharmacological suppression of REM sleep by amitriptyline leads – compared to placebo – to a reduced performance in a perceptual skill memory task, whereas in motor skill or declarative memory tasks there was no difference between conditions.

Altered Body Temperature Rhythm and Depression-like Symptoms following Early and Later Life Stress in Rats

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Objectives. In this study, animal models of early life stress were used to explore the impact of negative childhood experiences on behavioural outcomes as adults. We investigated consequences of long (LMS) and brief maternal separations (BMS) in early life followed by exposure to chronic mild stress (CMS) in adulthood on depressive-like behaviours and circadian rhythms.

Methods. Male rat pups were exposed to daily separations from the dam, during postnatal day (PND) 2-14 for either 180 min (LMS) or 10 min (BMS). At PND 90 animals were divided into 2 stress groups: LMS-CMS and BMS-CMS, and 2 control groups: LMS-CTRL and BMS-CTRL (n=20 in all groups). Animals in CMS groups were exposed to mild daily hassles for 4 weeks, while control animals were left undisturbed during the same period. Twenty-four hour preferences for sucrose and body weight were measured before and after CMS. Prior to CMS exposure, 8 LMS-CMS and 7 BMS-CMS animals were implanted with a subcutaneous telemetric device, and peripheral body temperature (BT) was recorded 48h before and after CMS protocol.

Results. Before CMS, no differences in body weight, sucrose preference and BT were present between adult LMS and BMS rats.
After exposure to chronic mild stressors in adulthood, LMS rats had lower body weight than BMS rats (p=0.025). Sucrose preference was reduced in LMS (p=0.004) but not in the BMS group. Telemetric data indicated several differences in BT. LMS had lower mean 24h BT compared to BMS, particularly evident in their inactive phases (p<0.001). Within the LMS group, the analyses showed a reduced mean 24h BT during both days after CMS (both p<0.001). Mean 12h BT was lower than before CMS during both the two light (both p<0.001) and two dark phases (both p<0.001). BMS had lower mean 24h BT during the first 24h after CMS (p<0.05) compared to baseline, but not during the next 24h.

Conclusions. The circadian rhythm of body temperature is disturbed after exposure to mild stressors over time in adult animals with a history of early life negative experiences (LMS). Reduced body weight and sucrose preference after stress exposure in these rats indicates the presence of depression-like behaviour. Adulthood stress exposure had no effects on BMS rats other than a transient reduction in BT. This confirms that LMS animals are more vulnerable to and have increased stress reactivity as adults, while BMS animals are more robust and may be able to cope more easily with challenges in later life.

A prospective descriptive analysis of head jerks during REM sleep

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Objectives. In a previous study, we found that head jerks are common during REM sleep (Brandauer E. Abstract Sleep Med. 2005). This finding was confirmed recently by other authors (Prieto-Prieto F. Abstract Sleep Med 2009). Aim of the present study was to systematically investigate head jerks during REM sleep in consecutive routine sleep laboratory patients.

Methods. Twenty-three patients (mean age, 52.7 ± 15.1 years) underwent at least one night of standard polysomnography including neck electromyography. If characteristic short movement artifacts were present, the synchronized video was inspected for the presence of head jerks. All head jerks were systematically characterized according to video-polysomnographic properties.

Results. Overall, 65 head jerks were registered during REM sleep. In the video, 56 out of 65 head jerks (86.2%) contained brief versions of the head, 10 out of 65 (15.4%) brief ventral flexions, and 29 out of 65 (44.6%) contained brief dorsal flexions of the head. Fifty-five of head jerks (84.6%) were associated with rapid eye movements, 48 (73.8%) were accompanied by muscle activitation in the chin EMG. Nine out of 65 (13.8%) head jerks were followed by arousals. Neck EMG activation was present in 61 (93.8%) of all head jerks. The mean head jerk duration defined by duration of neck EMG activation was 0,6±0.4 seconds. Thirty-five out of 65 head jerks had a duration shorter than 0.5 seconds (54%), whereas 30 had a duration longer than 0.5 seconds (46%). Mean EEG artifact duration was 0,6±0.4 seconds. Correlation between neck EMG and EEG artifact duration was very high ($rho=0.976$, $p<0.001$).

Conclusion. The short duration of head jerks indicates that they might belong to myoclonic phenomena. Neck EMG is activated with head jerks. Interestingly, length of neck EMG activation highly correlated to EEG artifact duration, which therefore not only provides a good marker for the presence, but also for the duration of head jerks.

Sleep-dependent memory consolidation in young healthy subjects: a fMRI study

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Objectives. Memory consolidation is enhanced by sleep and involves interactions between the hippocampus and neocortical areas. There is still a debate concerning the permanent or time-limited role of the hippocampus in memory retrieval, in particular when episodic and semantic memories are distinguished.
Using functional Magnetic Resonance Imagery (fMRI) and a total sleep deprivation paradigm, we investigated how sleep-dependent consolidation proceeds in young subjects and tried to precise the role of the hippocampus in memory retrieval.

Methods. 34 young healthy subjects participated in this study. They were invited to learn a series of emotional or neutral pictures. After learning, half of the subjects were totally sleep-deprived (TSD group) during the post-learning night while the other half slept at home normally (S group).
Memory retrieval was tested 3 days and 3 months after learning by means of recognition tasks associated to the Remember (R) / Know (K) paradigm. This latter allows the assessment of the subject's state of consciousness during memory retrieval. FMRI data were acquired during both recognition tasks and analyzed using SPM5.

Results. An ANOVA on memory performance with response type (R, K) and emotion (Negative, Neutral, Positive) as within subject factors and sleep group [S, TSD] and delay (3 days, 3 months) as between-subjects factor was performed. Recognition performance was equivalent between groups ($p= 0.22$) regardless of the delay. As expected, memory performance significantly declined with time ($p< 0.05$). Nevertheless, the group by delay interaction was not significant ($p = 0.34$) suggesting that subjects performed equally. The analysis of recognition performance with response type (R, K) and group at the 3day delay ($p = 0.14$) and the 3 month delay ($p = 0.13$) shows no significant interaction.
The analysis of fMRI data revealed a large common network activated by S and TSD participant when recognizing pictures. Interaction analyses disclosed differences between S and TSD groups, mainly in frontal and temporal areas.

Conclusion. Our results are in line with previous studies reporting different patterns of brain activity following sleep deprivation, despite a lack of obvious changes in behavior. Further analyses in the S group are conducted to better understand the role of the hippocampus for retrieving recent/remote episodic or semantic memories.

Evolution of objective, subjective and EEG measures of vigilance in patients with idiopathic hypersomnia during 40 hours prolonged wakefulness

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Objectives. Patients with idiopathic hypersomnia (IHS) suffer from disabling daytime sleepiness despite long and apparently undisturbed nocturnal sleep. The pathophysiology of IHS is unknown. The excessive daytime sleepiness (EDS) could reflect changes in homeostatic and/or circadian sleep regulatory processes. To investigate the underlying nature of EDS in IHS, we quantified the evolution of psychomotor vigilance, subjective sleepiness and EEG alpha activity during extended wakefulness.
Methods. Ten drug-naïve IHS patients (6 females; age: 17-58 years), diagnosed according to international criteria, and 10 matched healthy volunteers completed this case-control study. All participants were instructed to adhere to regular 16-hour wake/8-hour sleep schedule during 3 days prior to the study (monitored by actimetry). The protocol consisted of adaptation and baseline nights, 40 hours of constantly supervised wakefulness, and recovery night. During sleep deprivation, 10-min psychomotor vigilance task (PVT), Karolinska Sleepiness Scale, and standardized waking EEG recordings were administered at 3-hour intervals. PVT variables, subjective sleepiness, and EEG spectral power were analyzed with Matlab® and SAS®. Statistical analyses consisted of mixed-model ANOVA, two-tailed paired *t*-tests, and Wilcoxon signed-ranks tests.
Results. The Epworth Sleepiness Score before the adaptation night was higher in IHS patients than in controls (13.3±1.3 *vs.* 7.6±1.1, $p<0.02$). Throughout sleep deprivation, patients performed slower (mean and slowest 10th percentile of reaction times) and produced more lapses (transformed by $\sqrt{x}+\sqrt{x+1}$) on the PVT than the controls (ANOVA, 'group': $F>8.6$, $p_{all}<0.01$). By contrast, optimal PVT performance (fastest 10th percentile) did not differ ($F_{1,29.8}=1.6$, $p>0.2$). Subjective sleepiness (KSS) evolved differently in the two groups ('group' x 'session': $F_{13,90.3}=2.09$, $p<0.03$), revealing elevated sleepiness in the patients particularly during the first day of prolonged wakefulness. Similarly, relative 8-12 Hz activity was higher than in controls at 0.25 ($p<0.01$) and 3 hours ($p<0.03$) after waking from baseline sleep, but not thereafter ('group' x 'session': $F_{13,90.8}=2.74$, $p<0.003$).
Conclusion. Our data reveal complex differences between patients with IHS and healthy controls in the evolution of objective, subjective and EEG measures of vigilance during sleep deprivation. Ongoing analyses of sleep and sleep EEG before and after sleep deprivation may shed further light into possible mechanisms underlying EDS in IHS.

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Nocturnal Low Oxygen Saturation As A Main Factor Of Excessive Daytime Somnolence

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The main objective is to evaluate apnea-hypopnea index (AHI) and sleep time in oxygen saturation below 90% (Sat90) as predictors of subjective excessive daytime somnolence (EDS).

Polysomnographic recordings and Epworth Scale test were performed in 156 patients with suspected OSAS. Four groups were established according to AHI values: No OSAS (n=27), mild OSAS (n=51), moderate OSAS (n=36) and severe OSAS (n=42) when AHI was <5, 5-19, 20-49 or >50 respectively.

In our sample, Epworth Scale Score (ESS) does not interact with age, total sleep time, sleep latency, sleep efficiency, REM sleep or snoring index. Averages scores of Epworth scale by groups were 11.8, 11.8, 13.6 and 16.3 for no OSAS, mild OSAS, moderate OSAS and severe OSAS respectively (Kruskall-Wallis test, $p<0.01$). ESS is inversely related to Slow Wave Sleep amount (Fig.1) and REM sleep latency (Fig.2) (Spearman test, rho= -0.22 and -0.19 respectively, $p<0.01$ and 0.017), and directly with the AHI (Fig.3), Sat90 (Fig.4) and Arousal index (Fig.5) (Spearman test, rho=0.30, 0.33 and 0.23 respectively, $p<0.01$). In the male No OSAS group the ESS is associated to Sat90 (Spearman test, rho=0.65, $p=0.014$), but it is not with AHÍ (Fig.6).

Nocturnal oxygen desaturation is a mayor determinant of EDS among OSAS and male non OSAS patients.

The molecular basis of prion toxicity: Transcriptomics in an organotypic slice model

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Introduction. Transmissible spongiform encephalopathies (TSEs) are inevitably fatal neurodegenerative diseases that affect humans and a large variety of animals. These include Kuru, Creutzfeldt Jakob disease (CJD), familial fatal insomnia (FFI) in humans; scrapie in sheep; bovine spongiform encephalopathy (BSE) in cattle (Aguzzi 2008). The prevailing hypothesis states that the proteinaceous infectious particle, the prion, is the infectious disease-causing agent. The protein only hypothesis proposes that the prion consists of the scrapie-associated prion protein (PrP^{Sc}), an isoform derived by conformational change from the cellular PrP (PrP^{C}), a glycophosphatidylinositol(GPI)-linked membrane anchored glycoprotein. Prions most likely consist of an oligomer of PrP^{Sc} molecules that can catalyze the conversion of PrP^{C} into further PrP^{Sc} molecules and thereby propagate (*Prusiner, 1982; Weissmann, 1991*). Despite advances in our understanding of these mechanisms we still have only a very limited knowledge of how this disease-associated conversion leads to neurodegeneration (Aguzzi 2009).
Goal. Identification of pathways responsible for prion toxicity
Methods. The Aguzzi lab has established a method that allows for *in vitro* prion-infection of living brain slices prepared from mice (Falsig et al, 2008). Prion-mediated toxicity depends on the expression of PrP^{C} in the infected tissue as slices prepared from mice devoid of the cellular prion protein are resistant to prion replication and show no sign of neurotoxicity when treated with the infectious inocula. In addition, we have observed that treatment with anti-PrP antibodies induce neurotoxicity in a PrP-dependent manner. Preliminary microarray results from prion infected and anti-PrP antibody treated slices show that changes in gene expression occurs long before neurotoxicity and an increased gene-regulation is observed over time. We have identified several tool compounds that interfere with neurotoxicity without affecting prion replication, allowing us to dissect out neurotoxic pathways. As a next step we plan to perform a second round of microarrays on prion infected samples treated with 3 different compounds blocking neurotoxicity and one compound blocking prion replication. We will focus on genes that correlate with prion toxicity and are reversed by pharmacological inhibitors of toxicity allowing us to associate gene-changes with specific pathway or general pathways. We will validate changes in gene expression using nanostring technology and our biological findings on the RNA and protein level both *in vitro* and *in vivo*. A functional role of our candidates will be investigated by gene knockdown using Accell-siRNA (cell permeable siRNA), lentivirus or AAV virus in brain slices or by over-expression.and pharmacological manipulations will also be applied. Finally, if knockout/transgenic mice or pharmacological agents are available for candidate genes we will validate our results in vivo in prion infected mice.

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Event-related activity and phase locking during a psychomotor vigilance task

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There is profound knowledge that sleep restriction increases tonic (event-unrelated) electroencephalographic (EEG) activity. We tried to add a new perspective by identifying a possible relationship between phasic (event-related) EEG activity during a psychomotor vigilance task (PVT) and sleep pressure.

Twenty healthy subjects (10 male; mean age ± SD: 23.45 ± 1.97) underwent sleep deprivation for 24h. Subjects hourly had to rate their sleepiness (Karolinska sleepiness scale) and to perform a PVT while EEG was recorded simultaneously. Tonic EEG changes in the delta (0-4Hz), theta (4-8Hz), and alpha (8-12Hz) frequency range were investigated by power spectral analyses. Single trial (phase-locking index) and ERP analyses (P1, N1) were used to examine event-related changes in EEG activity.

Subjective sleepiness, PVT reaction times and tonic EEG activity (delta, theta and alpha spectral power) significantly increased over the night. In contrast event-related EEG parameters decreased throughout sleep deprivation. Specifically, the ERP component P1 diminished in amplitude as well as delta and theta PLI estimates decreased progressively over the night.

It is suggested that besides relying only on rather unspecific event-unrelated spectral power estimates (tonic EEG activity) event-related EEG activity (such as the amplitude of the P1 as well as delta/theta phase-locking) should be considered as new predictors for sleep pressure, arousal and attentional states of an individual.

Sleep promoting substances and stroke recovery

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Background. Ischemic stroke remains one of the leading causes of death in industrialized countries. Promoting neuroplasticity during recovery, in addition to thrombolysis and neuroprotection during the acute phase, may represent an alternative strategy in developing a new treatment for stroke patients. Clinical and experimental studies have suggested the importance of sleep in facilitating neuroplasticity. Sleep promoting drugs, such as gamma-hydroxybutyrate (GHB) and baclofen, have been shown to have the neuroprotective effect, when given within 24 hours after ischemia. In this study we intend to investigate the effects of GHB and baclofen given beyond the acute phase in a rat model of focal cerebral ischemia.

Aim. The main aim of this project is to examine the role of sleep in brain recovery after ischemic stroke in rats. This work is mainly focused on two issues: 1) Effects of GHB and baclofen on promoting sleep in the rat. This study will be carried out on healthy rats and GHB or baclofen will be given at different time points that are associated with changes in sleep pressure, such as the light and dark phase. 2) Effects of delayed treatment with GHB and baclofen on stroke outcomes.

Methods. Male Sprague-Dawley rats will be subjected to focal cerebral ischemia by occlusion of the distal branches of Middle Cerebral Artery (MCAo).Vigilance states will be monitored by recording of EEG and EMG. Infarction area will be evaluated by Nissl and Tunel staining. Functional outcome will be measured by the Single Pellet Reaching test (SPR). Neuronal survival will be assessed by several immunostainings. Quantitative RT-PCR and Western blotting analysis will be used to determine expression of neuroplasticity-related genes and proteins.

Expected results. Based on experimental evidence that sleep promotes neuroplasticity and on previous results demonstrated at our lab which have proven that sleep disturbances aggravate brain damage and impede functional recovery in rat model of ischemia, we expect GHB and baclofen to decrease infarct volume, improve recovery of motor activities and alter the expression of neuroplasticity-related genes.

Chronotypes and subjective sleep parameters in epilepsy patients: a large questionnaire study

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Objective. There is accumulating evidence that epilepsy and seizures may influence circadian rhythms and that circadian rhythms may influence epilepsy. It is also conceivable that seizure timing influences the timing of daily activities, sleeping and wakefulness (i.e. chronotype). Previously only one group has studied the distribution of chronotypes in people with epilepsy, showing significant differences between diurnal activity patterns in two groups of patients with different epilepsy syndromes.

Methods. To further investigate chronotypes in epilepsy, we performed a questionnaire based study to compare the distribution of chronotypes and subjective sleep parameters (sleep duration and time of mid sleep on free days) in 200 epilepsy patients to the distributions in the general population (n=4042). Within this large group of epilepsy patients, chronotypes of subsamples with well defined epilepsy syndromes (temporal lobe epilepsy (TLE, n=46), frontal lobe epilepsy (FLE, n=30) and juvenile myoclonic epilepsy (JME, n=38)) could be compared. In addition, twenty-seven patients who had had surgery for TLE were compared with those with TLE who had not had surgery. To determine chronotypes and subjective sleep parameters both the Morningness Eveningness Questionnaire and the Munich Chronotype Questionnaire were used.

Results. Significant differences in morningness/ eveningness distribution, timing of mid sleep (corrected for sleep duration) and total sleep time on free days were found between epilepsy patients and controls. People with epilepsy were more morning oriented, had earlier mid sleep on free days and sleep duration on free days was longer (p<0.001). However, distributions of chronotypes and sleep parameters between the groups of people with TLE, FLE and JME were not found to be different. People who had surgery for TLE had similar morningness-eveningness parameters and similar sleep durations when compared to those without surgery, but mid sleep on free days was earlier in operated patients (p=0.039).

Conclusion. This is the first large study focusing on chronotypes in people with epilepsy. We show that the distribution of chronotypes and subjective sleep parameters in epilepsy patients in general is different from that of healthy controls. Nevertheless, no differences are observed between patients with specified epilepsy syndromes, although they exhibit seizures with different diurnal patterns. Our results suggest that epilepsy in general, but not seizure timing, has a significant influence on chronotype behaviour and subjective sleep parameters.

Functional polymorphisms of DAT and COMT modulate slow wave sleep rebound after sleep deprivation in healthy humans

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Objectives. Most stimulants promote wakefulness by increasing dopaminergic neurotransmission. A role for dopamine in sleep-wake regulation, however, is not conclusively established. Synaptic dopamine activity is regulated by dopamine transporter (DAT) and catechol-O-methyltransferase (COMT). The functional Val158Met polymorphism of COMT strongly affects the efficacy of modafinil to mitigate impaired state and performance after sleep loss. To further investigate dopaminergic mechanisms in sleep-wake regulation, we examined whether variable number of tandem repeats (VNTR) of DAT and the Val158Met polymorphism of COMT epistatically affect the response to sleep deprivation.

Methods. The genotypes of the DAT 3' UTR VNTR and the COMT Val158Met polymorphisms were determined in 60 healthy adults, aged 19-35 years. All completed a protocol including adaptation and baseline nights, followed by 40 hours extended wakefulness, and recovery night. Baseline and recovery sleep, and subjective sleepiness (Stanford Sleepiness Scale) and sustained vigilant attention (PVT) during sleep deprivation were quantified. Data were analyzed with mixed-model ANOVA and unpaired, two-tailed t-tests.

Results. In baseline, slow wave sleep (SWS) differed among COMT genotypes ($F_{2,52}=4.5$, $p<0.02$), whereas all other sleep variables were similar in DAT and COMT genotypes (n=9-13 per group) in baseline and recovery nights.
Nevertheless, the increase in SWS after sleep deprivation was independently modulated by both DAT and COMT polymorphisms ($F_{1,52}=4.2$, $p<0.03$ and $F_{2,52}=9.20$, $p<0.004$, respectively). The SWS rebound was more pronounced in DAT 10-repeat allele carriers (67.0±17 min) than in 9/9- and 9/10-repeat allele carriers (52.8±20 min, $p<0.006$). Moreover, the increase in SWS was larger in COMT Val/Met heterozygotes than in both Val/Val and Met/Met homozygotes (71.6±23 vs. 56.1±17, $p<0.007$). By contrast, neither DAT nor COMT polymorphisms significantly affected the impact of sleep deprivation on sleepiness and PVT performance.

Conclusion. The SWS rebound after sleep deprivation is modulated by functional polymorphisms affecting dopaminergic neurotransmission.
Consistent with our previous results, Val/Val and Met/Met homozygotes of the Val158Met polymorphism of COMT did not differ from each other. The response to sleep deprivation, however, was smaller in both groups than in Val/Met heterozygotes. This finding suggests that similar to other brain functions, dopaminergic signalling modulates sleep homeostasis according to an inverted U-shaped response curve.

Effects of light supplementation on self-rated depression and sleep quality in older people living in care homes

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Objectives. To establish the effect of two different lighting conditions (blue-enriched versus control white light) on mood and self reported sleep of people living in care homes. The opinion of the participants on the different lighting conditions was also assessed.

Methods. Data collection was carried out in five care homes in the winter months from September 2008 to December 2009. The protocol was a randomised, crossover design. Each study period consisted of a baseline week (original care home lighting, (CH 4,5,6) ≈ 50 lux) and two, four week periods of light treatment (control white, 4000 K, ≈ 200 lux; blue-enriched white, 17000 K, ≈ 1000 lux) separated by three weeks of washout (care home lighting ≈ 40 lux). Lights were installed into selected communal areas and remained on all day. At baseline, the end of each light period and washout the participants (n = 38, 86.2 ± 1.1 yrs, mean ± SEM, 33 females, MMSE 19.6 ± 0.9) were questioned using the Geriatric Depression Scale (GDS) and were asked their opinion of the lighting condition on a 7 point scale (1, very unpleasant, 4 neutral, 7 very pleasant). A subset (n = 13, 84.8 ± 2.2 yrs, 11 females) also completed the Pittsburgh Sleep Quality Index (PSQI.) Data were analysed using repeated measures one way ANOVA with a Tukey post hoc test.

Results. There was no significant change in self-rated depression (GDS) between the baseline (global score 3.2 ± 0.4), washout (4.1 ± 0.5) and the lighting conditions (4000 K, 3.5 ± 0.5; 17000 K, 3.9 ± 0.5). PSQI scores were not significantly different between baseline (7.2 ± 0.9), washout (7.1 ± 1.0) and either lighting condition (4000 K, 5.6 ± 0.7; 17000 K, 7.2 ± 0.9). Participants did not indicate a preference for any of the lighting conditions (care home lights, 4.5 ± 0.2; 4000 K lights, 4.7 ± 0.2; 17000 K lights, 4.5 ± 0.3).

Conclusions. These preliminary data show that supplementation of blue-enriched or control white lighting in the communal areas of care homes does not affect self-rated mood or sleep quality and does not elicit a significant positive or negative response from the residents.

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Genome-wide association study identifies new HLA Class II haplotypes strongly protective against narcolepsy

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Objectives. Narcolepsy is a rare sleep disorder with the strongest HLA association amongst all HLA-associated disorders. Given that the associated HLA-*DRB1*1501-DQB1*0602* haplotype is common in healthy populations (15-25%), it was suggested that it is neither necessary nor sufficient for developing narcolepsy. Thus previous genome-wide association (GWA) studies of narcolepsy, as well as of most HLA-associated disorders, commonly ignored the HLA region.

Methods. We performed a GWA study in 562 European narcolepsy patients and 702 ethnically matched controls, with replication in independent samples of 370 narcolepsy and 495 controls, all carrying at least one *DRB1*1501-DQB1*0602* copy.

Results. We found association with a protective variant near the HLA-*DQA2* gene (rs2858884; $P < 3 \times 10^{-8}$). Further analysis revealed a surprising difference in heterozygous *DRB1*1501/1301* cases and controls, with cases almost never carrying a trans *DRB1*1301-DQB1*0603* haplotype (OR = 0.06; $P < 5 \times 10^{-4}$). We also replicated previously reported association at *TCRA* (rs1154155; $P < 2 \times 10^{-7}$).

Conclusion. This study by revealing a narcolepsy specific *DRB13-DQB1* haplotype reduces the associated HLA region down to a virtually unique involvement of a region containing *DQB1* and *DQA2* in narcolepsy susceptibility.

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Mobile Phone Battery Enhances Sleep Spindles

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Objective. Increasing evidence from electroencephalogram (EEG) studies suggest that electromagnetic fields (EMFs) emitted from mobile phones alter the sleep/waking neurophysiology. In a real mobile phone the EMF combines the radiofrequency (RF) electric fields transmitted and received via the antenna and the extremely low-frequency (ELF) magnetic fields stemming from the current drawn from the battery by the internal electronics. However, how much of the reported altering effects are due to the actual ELF magnetic fields and how much are due to artefacts from the RF near field exposure are yet to differentiate.

Methods. A GSM 900 MHz mobile phone was modified to separating the RF antenna from the phone's electronic components including the RF amplifier. This was then used for studying effects of the ELF magnetic field arising from the pulsating current from the battery supply (3.7 volts). The RF signal of the mobile phone was routed to a remote antenna situated 1.3 m away, pulse-modulated at 8 and 217 Hz by a base-station simulator. Ten healthy, right-handed male subjects (age: 21.4 ± 0.9y, range: 18-26y), sleep restricted to 6h, were exposed (blind) for 30 min to the ELF magnetic fields or sham signals (nil signal) at the right ear. The exposures was started at 13:30 at weekly interval with participants' states being monitored by continuous polysomnolographic (PSG) recording and subjective sleepiness reports in every 3 min. Immediately after each exposure, there was a 90-min sleep opportunity. The 90-min sleep structure (Rechtschaffen & Kales' criteria, 1968, EEG derivation C3-A2) was compared with sham mode using nonparametric Wilcoxon signed-rank tests.

Results. The sleep structure after the mobile phone ELF magnetic field exposure demonstrated a significant increased stage 2 duration (P=0.02), with no change in sleep latency (P=0.10), slow-wave sleep duration (P=0.39), sleep efficiency (P=0.12) or waking after sleep onset (P=0.68).

Conclusion. The current result implies that the mobile phone ELF magnetic field has a sleep maintaining effects. However, the manner it acts on sleep structure when coupling into the antenna RF signals may opposite the current findings according to previous findings.

A Neuropsychological Study of Executive Functions in Chronic Insomnia

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Objectives. Chronic insomnia is a prevalent health problem characterized by chronic complaints of nocturnal sleep disturbance and impaired daytime functioning. Although insomniacs complain of cognitive difficulties, objective deficits have been difficult to demonstrate. The aim of this study is to evaluate the difficulties of sleep, daytime functioning and executive functions in chronic insomnia.

Methods. The study comprised of two groups, 30 insomniacs and 30 controls, matched for age (26,80 ± 3,96 and 26,87 ± 4,60 respectively), sex, education level and chronotype. Sleep was monitored with wrist actigraphy, and the quantity and quality of the night's sleep was reported in a sleep diary. Neuropsychological assessment included tests of attention, working memory, verbal fluency, planning and decision making.

Results. The mean history of insomnia was 122,13 ± 89,43 months long. Insomniacs complained of multiple sleep-specific symptoms and non restorative sleep, which was corroborated by the actigraphic findings. No differences were found in tests of excessive daytime sleepiness (EDS), while insomniacs reported more fatigue. Significant differences were observed in tests of sustained attention, and working memory such as verbal and visual attentional span, maintenance, codification and manipulation of information as well as in the dual task paradigm. Moreover, insomniacs had difficulties regarding the inhibition of habitual but inappropriate responses as shown from their performance in the Stroop Task. As far as fluency is concerned, insomniacs generated fewer words according to both letter cues and category cues in verbal fluency tasks, whereas in the design fluency task, they failed to respect the rule imposed (4 lines/per design).

Conclusion. Chronic insomniacs suffered from a severe disorder presenting multiple sleep and waking symptoms. No symptoms of daytime sleepiness were observed, which confirms that insomniacs complain of fatigue, rather than of EDS. The neuropsychological data suggest that insomniacs present deficits in sustained attention, the executive control of attention, some components of working memory, verbal and visual fluency.

Anxiety – impaired sleep quality enhances homeostatic sleep pressure

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Objectives. There is evidence for an impaired sleep in pathological anxiety. Exploring sleep profile in animal models sharing relevant behavioural characteristics might be a useful approach to identify anxiety symptoms. To search for biological hallmarks in anxiety disorders, the present study examined changes in sleep architecture in the mouse model of trait anxiety screening high (HAB), normal (NAB) and low (LAB) anxiety-related behaviours.

Methods. Mice were implanted with EEG-EMG electrodes for polygraphic sleep recordings. Spontaneous sleep-wake states were monitored for a 24-h light-dark cycle starting with the onset of the light period. After baseline recordings, animals were sleep deprived by gentle handling for 6 h after the light onset. FFT analysis was applied to determine the power spectral profiles during NREM and REM sleep. The time-course changes in EEG delta power, averaged sleep-wake quantity and theta peak frequency were compared among three mouse lines.

Results. NAB mice displayed typical nocturnal variations in sleep and wakefulness, whereas LAB mice showed robust activity rhythm with remarkably shorter sleeping periods and long persistent periods of wakefulness during the active phase. The onset of sleep in LAB mice was delayed when compared to NAB or HAB mice. HAB mice showed greater sleep fragmentation, such as more frequent awakenings in-between with high numbers of short NREM and REM episodes. HAB mice were unable to maintain wakefulness for longer time periods, resulting in increased total sleep in the active period. EEG delta power was interminably elevated in HAB mice. Levels of REM sleep were similar between LAB and NAB mice, but elevated in HAB mice. Further, EEG theta oscillations were slower in HAB than in NAB and LAB mice. After 6 h of enforced sleep loss, LAB mice, in contrast to the other two strains, failed to increase EEG delta activity during NREM sleep.

Conclusion. The result indicates the direct influence of anxiety on sleep quality. Anxiety contributes to a disruption of sleep-wake cycle by frequent changes between status of sleep and arousal. Because of the inferiority of sleep affected by anxiety during the resting period, sleep demands may consequently increase during the active period. We therefore suggest that impaired sleep quality during anxiety leads to enhancement of homeostatic sleep pressure.

Hypersomnia associated with depression

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Introduction. Hypersomnia patients frequently suffer from depression. However, typical symptoms of hypersomnia could be confused with depression.

Aim. (1) to assess depression in narcolepsy with (NC+) and without cataplexy (NC-), idiopathic hypersomnia (IH) and controls (C).
(2) to compare depressive symptoms between narcoleptics and patients with a depressive episode.
(3) to identify the components of depressive symptoms of narcoleptic patients.

Method. Sixty-five NC+, 21 NC-, 15 IH patients, 36 outpatients with mild to moderate depression (D) and age and sex matched control groups participated in psychological testing. They completed Beck Depression Inventory (BDI), Zung Self-rating Depression Scale (SDS), Profile of Mood States (POMS), Global Impression of Severity of Depression (GSD) and Epworth Sleepiness Scale (ESS).

Results. Narcolepsy patients were significantly more depressed than controls in all scales. There were no differences in depression questionnaires between NC- and IH patients. Sex and a combination of antidepressants and stimulants, but not cataplexy were associated with depressive symptoms.
1. Narcoleptics scored lower on anhedonia in BDI. N and D were more impaired in POMS (total and all subscales) in comparison with C.
2. A factor analysis of BDI revealed that the component “negative attitude towards self” explained most symptoms of depression in N.

Conclusion. The findings support the assumption that the major psychosocial burden in narcolepsy is associated with sleepiness and not with cataplexy. Future studies should focus on the impact of medication on depression in patients with narcolepsy. N were less impaired in anhedonia, typically described as a core symptom of depression.

Association between fingers and images enhances the consolidation of procedural memory in serial reaction time task

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Objectives. Researchers in the field of memory have been interested in discovering factors that influence memory consolidation. Various studies examined the effects of sleep and emotion on memory consolidation. This study aimed to investigate if sleep and the presentation of negative, high valence stimuli would facilitate procedure memory consolidation.

Methods. 61 participants were presented with a modified serial reaction time task (SRTT) in four conditions where retention time (day/night) and stimuli type (neutral/negative) were manipulated. Participants were asked to memorise the association between 4 images, selected from International Affective Picture System database, and the fingers of their non-dominant hand except thumb and response to each image as fast and as accurate as possible. All the images of each set had either a neutral or an arousing emotional valence. Unknown to the participants, the order of presentation of the images followed a repeated sequence of 12 items. The experiment comprised two sessions – training and testing. The two sessions were separate for 12 hours. The training session had 30 blocks of 30 seconds SRTT. The testing session had 3 phases, SRTT with the same order of items in the first session, generation task and SRTT with random order of items.

Results. Results shown that participants in all the groups got faster and more accurate and there was no difference between the conditions. Some of the participants acquired explicit knowledge of the sequence. Response time and accuracy in both sessions for those participants were significantly better than the participants without explicit knowledge although the later participants also benefited from memory consolidation.

Conclusion. Having no difference between the conditions, shown that neither sleep nor negative emotional stimuli could enhance the memory consolidation. It might be because of the ceiling effect. The amount of improvement in different groups was comparable with the amount of performance enhancement reported in the literature for sleep group. The performance improvement in both the groups of participants who acquired explicit knowledge of the sequence and didn’t acquire explicit knowledge was comparable which shown memory enhancement happened for both groups of participants with implicit and explicit knowledge. This study suggests that engaging hippocampus enhances the consolidation of procedural memory.

Fingerprinting the sleep-related memory processing in the EEG spectra

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Objectives. The aim of the study was to identify changes in the all-night electroencephalographic (EEG) spectra which are specific for procedural and/or declarative sleep-related memory processing, while minimizing the effect of individual differences.

Methods. Twenty one healthy male subjects were recorded in the sleep laboratory with Alice 4 polysomnographic (PSG) system. Each subject was screened for four nights: 1) adaptation, 2) control, and 3-4) night with pre-sleep-task during which subject had performed either declarative or procedural task. The order of nights 2-4 was randomized. Recall performance was tested in the morning after the sleep. PSG data processing steps included visual sleep stage scoring and artefact removal. In each recording, mean log spectrum was estimated with Welch's periodogram for each electrode derivation and each sleep stage. Linear models and correlation coefficients were used to estimate the direction and compliance of power density (PD) change in separate frequency bins.

Results. Total sleep time as well as time spent in different sleep stages did not differ among nights 2-4 (one-way ANOVA, $p>0.05$). However, mean log spectra have revealed some distinctive differences. When spectra were analysed with linear models, a drop of PD relatively to the control night was evident throughout different derivations and stages, either in 'procedural' or 'declarative' nights. The largest drop in powers as well as the greatest difference between 'procedural' and 'declarative' spectra were detected within σ band, again for all derivations and stages. Positions of PD extremes (minima or local maxima) within this frequency band have revealed a complex pattern. The smallest interindividual variability, estimated by correlation coefficient, was observed in S2 stage at frontal and central positions, while the largest variability was detected at occipital derivations in general.

Conclusion. The results indicate that although experimental procedures did not significantly alter the sleep architecture, clear cut differences were found between control night and "procedural" or "declarative" night spectra.

Restless legs syndrome in patients with arterial hypertension

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Objectives. To perform a preliminary screening of restless legs syndrome (RLS) in patients with arterial hypertension (AH) and look for relation to affective symptoms and quality of life ratings.

Methods. Fifty-one patients with AH (38-79, mean=58.5 years, F-53.3%) were diagnosed AH according to European Society for Hypertension and European Society for Cardiology (ESH/ESC 2007) classification. Diagnosis of RLS was based on 4 essential criteria proposed by IRLSSG. Depression and anxiety were assessed according to Hamilton Depression and Anxiety Rating Scales (HAMD and HAMA). Quality of life was assessed by SF-36 generic questionnaire with 8 domains (D): D1 – physical health, D2 – role-limitations due to physical health, D3 – role-limitations due to emotional problems, D4 – energy/fatigue, D5 – emotional well-being, D6 – social functioning, D7 – pain, D8 – general health (all max 100). Evaluations were performed for 2 groups (AH with RLS and AH without RLS).

Results. Of the AH patients 14 (27.4%) were diagnosed as RLS supported by additional interview. According to HAMD and HAMA results 26 (51%) patients had moderate and severe depression and 18 (35.3%) moderate and severe anxiety. Depression prevailed in AH with RLS group (19.7vs.14.9, p=0.037). Analogous tendency was seen with anxiety, but not significant (25.8vs.20, p=0.1). SF-36 results were universally worse for AH with RLS group: D1-51.7vs.59.7, D2-6.2vs.36.1, D3-8.3vs.35.2, D4-41.7vs.47.5, D5-50vs.50.4, D6-63.5vs.63.9, D7-50.8vs.52.5, D8-40.4vs.41.7. Anyway, quality of life domains related to role-limitations in physical and emotional health were significantly worse in AH with RLS patients compared with non-RLS hypertensive patients (p=0.01 for D2, p=0.03 for D3).

Conclusion. Our results show higher rates of RLS in hypertensive patients compared to general population. Depression and anxiety were more marked in patients with concomitant RLS. Emotional and physical components of quality of life could be more impaired in AH patients with RLS. It is possible RLS could play a role in the course of AH by complicating affective disorders and influencing quality of life in patients with AH.

Vigilance in commercial vehicle operators

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Objectives. Daytime performance and alertness may be severely affected by sleep disturbances such as obstructive sleep apnea (OSA), insomnia and restless legs syndrome (RLS). They may therefore contribute to sleepiness and increased risk of falling asleep at the wheel. Our study addresses the prevalence of these conditions among commercial vehicle drivers and the effect of intervention.

Methods. Polygraphic recordings and questionnaires from volunteers recruited from a local bus and tram company (n= 116, male n=83, age median [range] 45[22-64] years) were assessed. Subjects with newly detected OSA participated in an interventional study addressing the effect of treatment. Polysomnography (PSG) and daytime vigilance function were assessed before and after treatment.

Results. The prevalence of subjective sleep disorders based on questionnaires assessed daytime sleepiness (Epworth Sleepiness Scale (ESS) 7[0-19]), insomnia severity (ISI score 10[0-26]) and RLS (IRLS 0[0-29]). Twenty two subjects were diagnosed with OSA AHI (n/h) 18[5-51] and received either CPAP (n=13), oral device (n=8) or a combination of both (n=1). Eight out of 22 subjects discontinued OSA treatment.
After treatment, the modified maintenance of wakefulness test (2x30 minutes) demonstrated an increase in median sleep latency from 22[17–30] to 30[13-30], p = 0.01) minutes. Sleep onset REM was not detected. The median AHI (n/h) decreased from 24 [4 – 81] to 2 [0 – 50], p = 0.01 and slow wave sleep (SWS, %) increased from 14[0-15.5] to 16[3–19], p=0.07. There was a significant negative correlation (p= 0.02, r = -0.89) between the difference in AHI and SWS. ESS decreased from 10.5[2 – 19] to 6.5[0 – 13], p= 0.003.
Diastolic and systolic blood pressure (mmHg) dropped from 88.5 [78-113] to 83[72-103] and 139[121-182] to 137[111-166], p = 0.02, p=0.05, respectively. No significant differences were seen in BMI and other sleep-PSG characteristics.

Conclusions. Sleep disorders were commonly found in this cohort of commercial vehicle operators. The number of subjects discontinuing treatment was high in patients with asymptomatic OSA. A significant improvement in subjective and objective hypersomnolence, blood pressure and an increase in SWS was seen post treatment.

Sensations and pain in restless legs syndrome

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Objectives. Restless legs syndrome (RLS) is a sleep related sensory motor disorder severely affecting 2-3% of adults. The aim of this study is to characterize the sensations and pain in RLS.

Methods. Fifty-six patients with idiopathic, treated RLS were interviewed face to face. The verbal descriptors (freely reported and chosen from the QDSA, a French reconstruction of the McGill Pain Questionnaire), and the topographical progression (between RLS onset and the present time of investigation) of the sensations in RLS, were analyzed. Measures also included demographics, RLS features, and scores on the international RLS severity scale, Pittsburgh sleep quality index, Epworth sleepiness scale, insomnia severity index, Beck depression inventory, and Pichot fatigue scale. Patients with and without painful RLS and those with spatially progressing versus stable RLS were subsequently compared.

Results. The patients (64 ± 11 years old; 37 women; 54 Caucasians) were 38 ± 17 years old at RLS onset, and had a severe RLS score: 21 ± 9. Most of them (84%) had a poor sleep, 41% had significant insomnia, 32% had an excessive daytime sleepiness, 29% had a mild to severe depression, and 11% were very tired. They freely qualified their sensations with 42 words (67% are found in and 31% have similar semantic meanings with the QDSA), including: "electrical" 43%, "prickling" 30%, "burning" 29%, "tingling" 27%, "irritating" 18%, "itching" 14%, "annoying" 11%, and "unbearable" 9%. The patients chose 10±3 QDSA words, covering all the QDSA groups and 95% of its words. The most frequently chosen sensory words were "irradiating" 55%, "electric shocks" 50%, "tingling" 36%, and "heat" 32%, while the most frequently chosen affective words were "unbearable" 48%, "irritating" 43%, "depressing" 39%, "distressing" 38%, "exhausting" 36%, "tiring" 32%, and "oppressive" 30%. After a median 25 years of RLS symptoms, half of the patients had a radical progression of their sensations to the upper limbs and were more frequently in pain, somnolent, tired and depressed than those patients with stable RLS. The patients with painful RLS (mostly since RLS onset) reported frequent burning sensations, a progression of RLS to the upper limbs with time, more somnolence and fatigue, and a more frequent use of opioids.

Conclusion. The sensations in RLS are very similar to pain descriptors, especially those of neuropathic pain, while painful RLS is a more severe and progressive phenotype.

Impaired glucose tolerance in sleep disorders

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Objectives. In the last decade several epidemiological and experimental studies on sleep have been performed and identified important contributions of sleep to various health outcomes and mortality. Some studies suggest a negative influence of shortened or disturbed night sleep on glucose tolerance. Despite the high prevalence of clinical sleep disorders no comparative studies of carbohydrate metabolism have been conducted.

Methods. We performed oral glucose tolerance tests (OGTT) and assessed additional parameters of carbohydrate metabolism in patients suffering from obstructive sleep apnea syndrome (OSAS, N=25), restless legs syndrome (RLS, N=18) or primary insomnia (N=21), and in healthy controls (N=33). The respective diagnoses were confirmed by polysomnography.

Results. Compared to controls, increased rates of impaired glucose tolerance were found in OSAS (OR: 4.9) and RLS (OR: 4.7) patients, but not in primary insomnia patients (OR: 1.6). In addition, HbA1c values were significantly increased in the same two patient groups. Significant positive correlations were found between 2-h plasma glucose values measured during the OGTT and the apnea-arousal-index in OSAS ($r = 0.56$; $p < 0.05$) and the periodic leg movement-arousal-index in RLS ($r = 0.56$, $p < 0.05$), respectively. Sleep duration and other quantitative aspects of sleep were similar between patient groups.

Conclusion. The present study for the first time compared glucose metabolism in various sleep disorders. The major finding is an increased rate of impaired glucose tolerance in patients with OSAS and RLS, but not in patients with primary insomnia, as compared to normal controls. Repeated arousals during sleep might be a pivotal causative factor deserving further experimental investigations to reveal potential novel targets for the prevention of metabolic diseases.

Patients with sleep breathing disorders have normal global cognitive function

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Objective. To assess the relation between sleep breathing disorders (SBD) and global cognitive function.

Methods. 117 hypertensive patients (mean age 55,2±11,5 years, 59% males) were enrolled. 79% of them had snoring and 52% hypersomnia according to questionnaire. 68% subjects had concomitant cardiovascular diseases (CVD) (56% - coronary artery disease, 47% had heart failure, 11% - cerebrovascular disease), and 21% had diabetes mellitus type 2. Sleep study was performed in all subjects. Cognitive function was assessed by Mini Mental State Examination (MMSE) test in the evening hours before sleep study.

Results. Based on the apnea-hypopnea index (AHI) patients were divided into groups matched by age, education, hypertension duration, and concomitant CVD prevalence: control group without SBD (n=17, AHI<5 per session hour), and subjects with SBD (n=100) that were subdivided into those with mild (5<=AHI<15, n=35), moderate (15<=AHI<30, n=21) and severe SBD (AHI=>30, n=44). MMSE scores in groups were 26.8±1.4; 27.1±1.4; 25.8±3.5, and 27.9±1.6, respectively (p=0.002), but no significant difference was found between SBD and non-SBD patients (p=0.11). Based on pairwise comparison patients with severe SBD had higher MMSE scores than those with moderate SBD (p=0.008) and without SBD (p=0.002), but there was no difference between other group pairs (p>0.05). 71% non-SBD and 45% SBD subjects showed a decreased MMSE score (p=0.06), but 73% patients with severe SBD had normal cognitive score. MMSE scores positively correlated to SBD severity (r=0.28, p=0.002, Spearman analysis) (both with AHI - r=0.26, p=0.005, and desaturation index (ODI) - r=0.25, p=0.007), thus, patients with more severe SBD have better global cognitive function. MMSE score positively correlated to educational level (r=0.28, p=0.003) and negatively – to age (r=-0.33, p<0.001), and after adjustment for these variables the correlation for AHI and ODI disappeared (r=0.19, p=0.07 and r=0.14, p=0.19, respectively). When dividing subjects by age threshold of 55 years MMSE score correlated to educational level (r=0.384, p=0.005) in a younger subgroup and did not correlate to SBD severity indices if adjusted for education.

Conclusion. Patients with SBD and concomitant CVD show no global cognitive decline as compared to controls. Subjects with severe SBD demonstrate even better cognitive function that seems to be more related to educational level and age rather than to desaturation and apnea-hypopnea indices.

Keywords. Sleep breathing disorders, sleep apnea, cognitive function, cognitive decline.

Induction of hippocampal theta rhythm after amphetamine microinjection into the ventral tegmental area in the rat

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Objectives. Hippocampal theta rhythm is characteristic of paradoxical sleep and of certain waking behaviours such as exploration. The midbrain ventral tegmental area (VTA) might belong to the structures involved in the regulation of hippocampal theta. In our previous study, we found that procaine injection into the VTA, as well as its electrolytic lesion, produce suppression of this type of EEG activity. However, the VTA consists of a number of neurons, among which the dopaminergic and the GABAergic cells form the main part. In order to assess the participation of particular neurotransmitters of the VTA in the regulation of hippocampal electric activity, direct pharmacological manipulations toward specific receptors should be employed. We have found that blockade of GABA A receptors within the VTA (bicuculline microinjection) induces long episodes of hippocampal theta, whereas stimulation of this kind of receptors (muscimol microinjection) blocks the possibility of theta elicitation
with sensory stimulation. The present study aimed at estimation of the influence of the
dopaminergic system of the VTA on hippocampal theta, by the means of direct unilateral amphetamine (AMPH) microinjection into the VTA.

Methods. The research was conducted on 5 male Wistar rats maintained in deep urethane anaesthesia. In such conditions, slow irregular large amplitude activity is seen in hippocampal EEG and theta can be elicited by sensory stimulation (tail pinch lasting for 1 min, delivered at intervals of 10 min). Amphetamine was administered at a dose of 5 micrograms and at a volume of 0.5 microL. As a control injection, sodium chloride was administered into the VTA at the same volume.

Results. After amphetamine microinjection, we could observe appearance of spontaneous theta rhythm in the hippocampal recording without applying the sensory stimulation. The change of hippocampal EEG was also apparent in the FFT analysis of 5-s recording samples. The analysis showed increase in peak power at theta band (3 – 6 Hz) with a simultaneous decrease in delta band (0.5 – 3 Hz). One-way ANOVA showed significant differences already 10 minutes after AMPH administration. Hippocampal EEG returned to the control conditions within 80 minutes after AMPH injection.

Conclusion. As amphetamine intensifies dopaminergic action, we speculate that it is the dopamine system within the VTA that is involved in the elicitation of hippocampal theta. We assume that the dopaminergic neurons in the VTA are under tonic inhibitory influence of GABA A receptors, which can explain our previous results pertaining to GABA A system. Whether these are the direct or non-direct connections between the VTA and the hippocampal formation that are crucial for theta regulation, remains to be solved.

The Daytime Functioning and Sleep Attribution Scale (DFSAS): A new insomnia-specific measure to probe daytime impairment and poor sleep attributions

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Introduction. Current assessments of daytime functioning and quality of life in insomnia rely on tools which are generic and non-specific (e.g. SF-36), or designed to assess a single construct (e.g. depression), or just single non-validated items. The challenge in creating an insomnia-specific scale relates to the influence of co-occurring conditions. Here we present preliminary data on the daytime functioning and sleep attribution scale (DFSAS), a two part measure designed to assess impairment in daytime domains commonly reported by individuals with insomnia (part 1), and, importantly, sleep-related attributions in accounting for such reported daytime impairment (part 2).

Methods. Thirty-nine individuals with primary insomnia (PI), according to DSM-IV criteria, and 31 normal sleepers completed the DFSAS. A sub-set (n=18) of the PI group completed the DFSAS during a brief 4-week sleep restriction therapy intervention, enabling assessment of sensitivity to change. We report data on internal consistency, discriminant validity, concurrent validity, and sensitivity and specificity.

Results. DFSAS items were selected based on focus group and audio-diary data collected during a previous investigation. Parts 1 and 2 successfully discriminated PI individuals and normal sleepers (both $p<.001$). Both parts 1 & 2 had high sensitivity and specificity (>87%). Cronbach's alpha was 0.81 for part 1 and 0.89 for part 2. DFSAS scores (part 1) were positively associated with insomnia severity (ISI; *rho*=.49) and occupational impairment (OISQ; *rho*=.76), and negatively associated with several SF-36 dimensions, including vitality (*rho*=-.51), general health (*rho*=-.54) and emotional role limitations (*rho*=-.43). DFSAS part 1 and 2 scores significantly improved over the course of sleep restriction therapy, and these changes were associated with improvements in sleep diary variables.

Conclusions. Preliminary data indicate the DFSAS to be valid, internally consistent, and sensitive to change. The attributional component of the DFSAS adds a new dimension to the assessment of daytime functioning in insomnia, and also permits use with co-morbid insomnia populations. Further testing with larger samples is required.

Networks within and between the basal forebrain, hippocampus and prefrontal cortex - in a model for depression caused by disturbed sleep

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Disturbances in sleep are encountered in the majority of patients with depressive disorder. To elucidate the molecular mechanisms behind this relationship we examined gene expression changes in a rodent model for disturbed sleep and depression. The animals were treated with daily injections of clomipramine in their early infancy, after which the changes in gene expression was examined using the Affymetrix Rat 230.2 chip. We studied the gene expression in the basal forebrain, hippocampus and frontal cortex and combined the results to reviele the otherwise indissectible networks between the tissues.
The major disturbed pathways involved translational regulation, synaptic transmission and axon components.
A network analysis, allowing for additional interactors revieled a disturbed communication between the different brain areas. The results from the network analysis also suggest possible mechanisms behind the disturbed communication.

Stimulation of anterior gingulate gyrus and modulation of pain

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Introduction. Functional imaging studies suggest an involvement of the rostral (perigenual) cingulate gyrus in both pharmacological and neurostimulation analgesia (precentral cortex, ventrocaudal talamus, spinal cord). Direct stimulation of this region might consequently become a therapeutic option in patients with pharmacoresistant neuropathic pain. Stimulation of the perigenual anterior cingulate cortex (PgACC) is currently used in the treatment of resistant depression. The aim of this study, still in progress, is to assess the effects of PgACC neurostimulation on the perception of pain in patients chronically stimulated to treat endogenous depression.

Methods. We present the results gathered in the two first patients who underwent the study. A first subject was assessed three times, before and twice after chronic implanted stimulation of the perigenual cortex. The second patient was studied only after chronic stimulation, with the stimulator “on” and “off”. Variables assessed were the perception and pain thresholds to sural nerve stimuli, as well as the threshold of the associated flexion (RIII) reflex and the tolerance to cold pain on the “cold pressor” test.

Results. In the patient studied before and after stimulation, the latter entailed a notable increase of the nociceptive reflex threshold (from 20±2 to 30±5 mA), as well as an increase of the tolerance in the cold pressor test (from 17 sec to 38 sec). Discontinuation of PgACC stimulation during 10 minutes decreased cold pain tolerance to 20 sec, without sizeable modification of the nociceptive reflex. Although the second patient was not studied before operation, a similar pattern was observed following chronic stimulation of the CCPp, with enhancement tolerance to the cold pressor test (45 sec) and high threshold of nociceptive reflexes (26 mA).

Conclusion. In these two first patients stimulation of the cingulate gyrus increased the tolerance to cold pain and attenuated the nociceptive RIII reflexes. Whether or not these preliminary results reflect a general analgesic tendency of PgACC stimulation can only be confirmed by the study of a larger sample of patients.

HPA axis function in primary insomnia, sleep apnea and restless legs syndrome

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Objectives. Disturbed function of the hypothalamic-pituitary-adrenal (HPA) axis is reported in sleep disorders. In primary insomnia, the dysfunction of the HPA axis is supposed to play an important pathophysiological role. However, most studies measured 24h-blood or urine cortisol levels. A sensitive challenge test to evaluate dynamic response of the stress hormone system like the dexamethasone-suppression/corticotropin-releasing-hormone-stimulation test (DEX/CRH-test), a well established test in depression, was never used.

Methods. To assess effects of chronic sleep disorders on negative feedback sensitivity of the HPA-axis we compared 25 obstructive sleep apnea (OSA) patients, 18 restless legs syndrome (RLS) patients, 21 primary insomniacs with 33 healthy controls. Probands underwent the DEX/CRH-test which combines suppression (by dexamethasone) and subsequent stimulation (by CRH) of cortisol secretion.

Results. The number of non-suppressors (baseline-cortisol ≥ 40ng/ml) did not differ among groups indicating normal negative feedback sensitivity. Furthermore there were no group differences in CRH stimulated ACTH or cortisol secretion or the adrenocortical reaction on ACTH.

Conclusion. For the first time we could report that patients with OSA, RLS and primary insomnia do not show dynamic alterations of the HPA-axis. Results suggest that chronically disturbed sleep does not affect negative feedback sensitivity. It seems that stress system pathology which might exist in chronic sleep disorders is independent of negative dynamic regulation processes of the HPA-axis system.

Indications of mandibular advancement ortheses in the treatement of excessive daytime sleepiness caused by positional supine apnea

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Mandibular advancement devices represent a therapeutic option for obstructive sleep apnea syndrome (OSAS), upper airway resistence syndrome and snoring. The effect of these ortheses on the positional supine apnea is not well documented

Study objective. Impact of mandibular advancement ortheses in the treatement of daytime sleepiness.

Design. retrospective et prospective study

Material and methods. Sleep recordings were performed in 20 patients with excessive daytime sleepiness (EDS), in two conditions: with and without mandibular advanced ortheses. Among these patients, 15 had been diagnosted with obstructive sleep apnea with a median apnea-hypopnea index (AHI) of 20/hour and 5 patients with AHI less than 10/hour, but with a strong impact of EDS on daily functioning (cognitive and motor activities). The positions facilitating the respiratory phenomena have been quantified.

Results. Clinical improvement has been noticed in all the EDS patients with severe AHI and in 40% of the EDS patients with a small AHI, following the mandibular advanced orthesis use. The use of the orthesis also modified sleep arhitecture in all patients with obstructive sleep apnea, by increasing the time spent in deep sleep stages and decreasing the arousal index. The median AHI has also decreased with 64% as comparing to the condition without orthesis in these patients. Furthermore, it has been noticed that the patients with the most severe positional apnea had the biggest benefit from the ortheses use.

Conclusions. Our study shows that the mandibular advancement ortheses has a clear positive impact on the patients with obstructive sleep apnea in the supine position, by reducing AHI index and improving sleep quality, whereas in the EDS patients with a low AHI, the use of ortheses may be potentially encouraging.

Light effects on sleep, activity and daytime mood in older people with sleep problems

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Objectives. To study the effects of 2 polychromatic white lights of different spectra (blue-enriched, 17000K vs. control, 4000K) at 2 intensities (~400, 1100 lux), on sleep, alertness and mood in older people (≥ 60 years) with self-reported sleep problems (Pittsburgh Sleep Quality Index > 5).

Methods. 33 healthy volunteers (66.5 ± 4.7 yrs; 23F, 10M) participated in an at-home study of 11 weeks: 1 week baseline, 3 weeks daily light exposure (2h in the morning and 2h evening), followed by 2 weeks of washout for each light condition (randomised, crossover design of 17000K and 4000K lights). 12 subjects received 17000K and 4000K low intensity lights (~$3.6x10^{14}$ photons/cm^2/sec), 21 subjects received 17000K and 4000K high intensity lights (~$9.1x10^{14}$ photons/cm^2/sec). Subjects completed daily sleep diaries, mood and alertness scales, and wore an activity monitor (Actiwatch-L) to assess sleep and circadian activity levels using non-parametric circadian rhythm analysis (NPCRA) parameters (IS, IV, M10 onset). The urinary metabolite of melatonin, 6-sulphatoxymelatonin (aMT6s), was measured before and at the end of each 3-week light exposure period (via sequential urine collection over a 39h period) to assess circadian phase and amplitude.

Results. The light data were corrected for baseline and the effects of light treatment (17000K vs. 4000K light), light intensity (low vs. high) carry-over and period (first vs. second light exposure) were measured using PROC GLM. Subjective attempted sleep start time and actigraphic sleep onset time were significantly later with the blue-enriched light compared to the control light (irrespective of intensity). Low irradiance light (~400 lux) significantly reduced the duration of actigraphic night awakenings and fragmentation, increased sleep efficiency and night immobility, advanced sleep onset and the M10 onset time (irrespective of light condition). The second exposure period produced a significantly later aMT6s acrophase time and improved IS and IV. No significant changes were found for mood and alertness parameters.

Conclusion. Timed light exposure showed some effects on sleep, activity parameters and circadian phase in older people with sleep problems.

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Sleep homeostasis in the rat during chronic sleep restriction

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Objectives. Sleep is homeostatically regulated in all mammalian and non-mammalian species that have been carefully studied so far. In mammals and birds, the best characterized marker of sleep homeostasis is slow wave activity (SWA), the EEG power between 0.5 and 4 Hz during NREM sleep. SWA reflects the accumulation of sleep pressure as a function of duration and/or intensity of prior waking: it increases after spontaneous wake episodes and short-term (3-24 h) sleep deprivation and decreases during sleep. However, some studies have raised doubt about the ability of SWA to reflect sleep need after chronic sleep deprivation or sleep restriction (SR). Moreover, recent evidence suggests that sleep may be regulated by both allostatic and homeostatic mechanisms under conditions of chronic SR.

Methods. Here, we performed continuous, virtually artifact-free EEG recordings from frontal, parietal and occipital cortex in freely moving rats (n=11) during and after 5 days of SR. During SR, rats were allowed to sleep during the first 4 hours of the light period (4S+) but not during the following 20 hours (20S-).

Results. During the daily 20S-, NREM sleep was reduced by ~80%, and consisted mostly of short sleep attempts <20 s (mean duration 10.3 ±0.1s). Low frequency EEG power (1-6 Hz) in both sleep and wake during 20S- periods was increased by 20-40%, most notably in occipital cortex. Although SR did not markedly affect the amount of NREM sleep during S4+, higher sleep pressure was apparent in increased sleep consolidation (~30% increased NREMS episode duration, ~50% fewer brief awakenings) and shorter sleep latencies (from ~25 min to <10 min) on all SR days.
In all animals, NREM SWA sleep increased above baseline levels by ~20% during the 4S+ periods and in post-SR recovery. This increase was most pronounced in frontal cortex, and was strongly determined by the efficiency of SR. Thus, the number of sleep attempts during 20S- correlated positively with subsequent NREM SWA ($r=\sim0.4$, $p<0.05$), while wake SWA during 20S- correlated negatively with subsequent NREM SWA ($r=-0.81$, $p<0.001$).
Analysis of cumulative slow wave energy (SWE = SWA x time) demonstrated that the loss of SWA during SR was compensated by the end of the second recovery day after SR.

Conclusion. These results show that the homeostatic regulation of sleep is preserved under conditions of chronic sleep restriction.

Applicability of shift-work protocols in rats; effects on body weight gain, behavioural activity and instrumental learning

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Recently, shift-work has been elegantly modelled in rats by exposing them to forced locomotion for 8h per day (weekdays only) during their inactive phase over a period of four weeks. Consistent with human shift-workers, shift-working rats had alterations in the rhythmicity of food intake, glucose rhythmicity and body weight gain.[1] We investigated if the used protocols could also be implemented with a different type of apparatus for forced locomotion.

Work was modelled by 8h of mild forced locomotion for 5 days / week (weekends off). We exposed 32 rats to one out of four conditions; work during the active phase under reversed light conditions (WORK), home cage control under reversed light conditions (WORKCON), Work during the inactive phase under normal light conditions (SHIFTWORK), and a normal light home cage control (SHIFTCON). Weights were monitored during baseline and 5 weeks of work.

In contrast with previous findings, shift-work decreased the normal weight gain from 123g (±15) to 76 g (±8) instead of increasing it. We explain this finding with the concurrent observation that our SHIFTWORK rats do not decrease their home-cage activity between shift-work, which they did in the previous study. WORK did not alter body weight gain (85g ±11) when compared to WORKCON (84g ±11). Next to metabolic changes, shift-work induces cognitive impairments in humans.[2] The rodent shift-work model may also induce cognitive impairments. We therefore tested if work and / or shift-work altered learning of a simple goal-directed behaviour; the association of lever pressing with food reward (Instrumental learning). Rats were trained on an instrumental learning paradigm during the fifth week of the experiment, in 6 sessions over the course of 3 workdays (Wednesday–Friday). None of the conditions affected instrumental learning. All four groups showed equivalent increases in lever pressing from the first (3.8 ±0.7) to the sixth (21.3 ±2.4) session, and needed a similar amount of sessions (5.1 ±0.3) to reach a learning criterion (>=27 out of 30 lever presses). After 5 weeks of exposure to work, rats may have become too habituated to this protocol for learning to be affected.

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Sleep-dependent daily changes in blood pressure in leptin-deficient obese mice

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Objectives. Blood pressure (BP) shows a 24-hour rhythm, decreasing substantially on passing from the daily period of activity to that of rest and sleep. The daily rhythm of wake-sleep state (wakefulness, W, non rapid-eye movement sleep, NREMS, rapid eye movement sleep, REMS) may play a causal role in determing the daily rhythm of BP because BP is substantially higher in W than either in NREMS or REMS. The leptin hormone is a key modulator of the hypothalamic pathways that control energy homeostasis. Mice homozygous for a nonsense mutation in the leptin gene (ob/ob mice) are leptin deficient, severely obese, and show altered daily rhythms of wake-sleep states and BP. We investigated whether differences in BP between ob/ob mice and their controls depended on interacting effects of the wake-sleep state and the time of the day.

Methods. Ob/ob mice (B6.V-Lep^{ob}/^{ob} OlaHsd strain, n = 7) and their lean wild-type littermates (+/+, n = 10) were kept on a light-dark cycle of 12-h periods with ambient temperature of 25℃ and free access to food and water. After extended (10 days) postoperative recovery, BP (TA11PA-C10 telemetric transducer, DSI) and electroencephalographic and electromyographic signals (cable transmission) were recorded for 72 hours with mice undisturbed and freely moving in their own cages. W, NREMS and REMS were discriminated on 4s epochs. For each wake-sleep state, mean BP value was computed on episodes longer than 60 seconds and averaged as a function of time of day (8 consecutive time bins of 3 hour duration). Data were analyzed with 3-way analysis of variance (ANOVA, with wake-sleep state, time bin and genetic group as factors) and t-test (significance, $p<0.05$).

Results. BP showed a significant interaction effect among wake-sleep state, time bin and genetic group. In W, BP was significantly higher in ob/ob than in +/+ mice in all time bins. In NREMS, BP was significantly higher in ob/ob than in +/+ mice only during the last 3 time bins (i.e., 9 hours) of the light (rest) period. In REMS, BP did not differ significantly between groups in any time bin.

Conclusion. These results indicate that in the absence of leptin, obesity may entail hypertensive derangements in BP that depend on interacting effects of the wake-sleep state and the time of day.

Keywords: blood pressure, daily rhythm, obesity.

Assessment of sleep-wake behaviour in disorders of consciousness

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Objectives. The characteristics of sleep-wake behaviour in patients with severe brain damage has not been extensively investigated and remains poorly understood. Damage seen in disorders of consciousness, such as “Persistent Vegetative State” (VS) and “Minimally Conscious State” (MCS), is generally accompanied by changes in electrical brain activity. However, analysis of the sleep and wake electroencephalogram (EEG) in these patients is lacking with only few case studies reported. Furthermore, large discrepancies in observations exist, and the methodology has suffered from several important weaknesses. One major consideration is whether scoring based on standard criteria is appropriate due to the severe EEG alterations associated with brain damage. Therefore, in view of these shortcomings and to improve future diagnosis and prognosis, there is an urgent need for systematic sleep-wake behaviour assessment in these patients.

Methods. Three ~24h polysomnographic recordings were collected in 3-week intervals as part of a collaborative project designed to assess verticalisation treatment on various physiological parameters in VS and MCS patients. Nine patients (4 males, 5 females) between 18 and 63 years (mean ±SEM: 43.9 ± 4.5y) were evaluated. All data were visually scored in 20-s epochs. As anticipated, scoring according to standard criteria was not appropriate and therefore new criteria were developed according to commonalities in physiological signals across patients.

Results. Patients exhibited similar physiological patterns across all recordings, however, a high variability between patients was observed. The most striking feature across patients was a general slowing of the EEG. Although all patients appeared to have sleep and wake-like states, none showed a clear sleep-wake cycle. Typical EEG signatures of sleep such as sleep spindles or K-complexes were virtually absent. However, in one patient there was a clear period of sleep that was abundant with sleep spindles, and interestingly, this was the only patient that emerged from the VS during the study period.

Conclusion. Sleep-wake-like-behaviour in VS and MCS does not show a common pattern across patients and accordingly, scoring based on standard criteria is inappropriate. Additionally, the results suggest spindle activity may provide an insight into disorders of consciousness. More data is needed to establish specific scoring rules and further explore sleep-wake-like behaviour in these patients.

How important is disturbed sleep for the patient with Parkinson's disease?

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Objects. Sleep disorders are among the most frequent non-motor symptoms in Parkinson's disease (PD). We analyzed treatment priorities of PD patients, to assess the relative burden of sleep disturbances compared to other symptoms.

Methods. We studied a cohort of PD patients, who were referred for an assessment in the Parkinson Centre Nijmegen, a tertiary academic referral centre. Before their visit, patients were asked to rank a top 5 out of 23 items, indicating the problem areas they definitely wanted to be addressed during their visit. Among other variables, nocturnal sleep quality and excessive daytime sleepiness were assessed with validated questionnaires.

Results. A total of 317 patients completed the questionnaires (192 men). The mean age (±SD) was 66.1 ± 9.5 years, with a mean disease duration of 7.8 ± 6.4 years. Mean score of the Pittsburgh Sleep Quality Index (PSQI) was 6.9±3.9, disturbed nocturnal sleep (indicated by a PSQI>5) was present in 184 patients (58.0%). Mean score of the Epworth Sleepiness Scale (ESS) was 6.22±4.6, excessive daytime sleepiness (ESS > 10) was present in 52 (16.7%). A total of 127 patients (40.1%) prioritized sleep as an item to be discussed during their visit. Overall, sleep was the 6th item of importance, and from the non-motor symptoms, only memory scored higher (141 patients, 44.5%). Patients who scored sleep as a priority had significantly worse nocturnal sleep quality (PSQI 9.2 ±3.9 vs. 5.4 ±3.0; $p<0.001$). From those with a PSQI > 5, 87.7% scored sleep as a priority (Chi-square 52.8; $p<0.001$). ESS scores were not different between patients who prioritized sleep and those who did not.

Conclusion. Sleep disturbances are an important issue for PD patients, especially among the non-motor symptoms. Disturbed nocturnal sleep was the primary reason for patients to demand medical attention.

Autonomic dysfunction in patients with obstructive sleep apnea-hypopnea syndrome

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Background. Obstructive sleep apnea-hypopnea syndrome (OSAHS) is characterized by repeated partial or total airway collapse during sleep, causing oxygen desaturations, autonomic stimulation, sleep fragmentation and potentially fatal cardio-metabolic consequences. Variations in pulse transit time (PTT) reflect the autonomic response to apneas.

Aim. the evaluation of autonomic dysfunction in patients with OSAHS, using PTT and heart rate (HR) as autonomic parameters.

Patients, methods. 12 patients with mild OSAHS (apnea-hypopnea index AHI = 8.06 ± 1.56), 10 patients with moderate OSAHS (AHI = 21.2 ± 5.8), 9 with severe OSAHS (AHI = 54.78 ± 7.91) and 9 subjects without apnea (IAH < 5) were included in the study after complete polysomnography including cardio-respiratory and neurophysiologic sleep monitoring. The heart rate coefficient of variation was calculated by the polysomnography software (CV calc) by deviding the standard deviation by the mean. PTT represents the interval between the R wave on ECG and the pulse wave on pulse-oxymetry and PTTv is the PTT variation during apneas. We have also assessed manually the heart rate coefficient of variation on sampled apnea-free epochs in all sleep stages (CV man) and the heart rate response to apneas (ΔFC).

Results. Both CVcalc and CVman were lower in the severe OSAHS group compared to the mild OSAHS group and the apnea-free group ($p < 0.01$) and they correlated inversely with AHI ($r = -0.81$ for CVcalc and $r = -0.72$ for CVman), only in non-REM sleep. PTTv and Δ FC also norrelated negatively with AHI ($r = -0.79$ and -0.58, respectively).

Conclusions. Autonomic response to apneas is impaired in patients with OSAHS, proportionally with the severity of OSAHS. Heart rate variability is diminished in patients with severe OSAHS, even in apnea-free periods in non-REM sleep.

Keywords: apnea, autonomic, pulse transit time

Changes in cardiovascular parameters during REM sleep in rats exposed to different ambient temperatures

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Objectives. REM sleep (REMS) is characterized by the suspension of thermoregulation and by an instability of autonomic cardiovascular parameters such as arterial pressure (AP), heart rate (HR) and cutaneous vasomotion (1). Aim of this study was to investigate the relationship between cardiovascular regulation and thermoregulation during REM sleep by analysing cardiovascular changes during REMS in animals kept at different ambient temperatures (Tas).

Methods. 6 Male CD rats were adapted to normal laboratory conditions (Ta: 25±1℃; Light-Dark cycle 12h:12h) and implanted wit h: i) electrodes for EEG and EMG recording; ii) a femoral catheter for AP and HR determinations. An infrared camera was used to measure tail temperature (Tt). Animals were studied for 3 consecutive days at Ta 32℃, 25℃, an d 4℃. Changes in systolic AP (sAP, mm Hg) and HR (bpm) values were calculated as the difference between the value of the median and that of either the 95th percentile (increments, P95) or the 5th percentile (decrements, P5) of the whole population of instantaneous values collected during different REMS episodes.

Results. Preliminary results show that during REMS: i) Tt decreased (-0.28 ± 0.06 ℃) about 60s from the start of an episode at Ta 32℃, while no appreciable changes were observed at 25℃ and 4℃; ii) changes in HR were characterized by decrements larger than increments at Ta 4℃ (P5= 80; P95= 36), by increments slightly larger than decrements at Ta 32℃ (P95= 51; P5= 41), and by similar changes at Ta 25℃ (P95= 59; P5 = 61); iii) increments in sAP were larger than decrements at any Ta (Ta 4℃: P95= 15, P5= 12; Ta 25℃: , P95 = 15; P5= 11; Ta 32℃: P95 = 15, P5 = 9).

Conclusions. REMS related changes in Tt and sAP appear to be independent from changes in Ta and suggest that REMS is characterized, at both low and high Ta, by a sustained sympathetic outflow to vascular system. Conversely, changes in HR are characterized by a distinct prevalence of a relative bradycardia at low Ta and by a slight prevalence of a relative tachycardia at high Ta. In conclusion, it would appear that the impairment of thermoregulation during REMS induces correspondent changes in HR but not in the vascular system, which is kept under the action of a tonic sympathetic drive.

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Theory of mind and executive functions in Attention Deficit Hyperactivity Disorder (ADHD)

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Objectives. Besides behavioural disorders, Attention Deficit Hyperactivity Disorder (ADHD) characterizes by cognitive impairments, mainly in attentional and executive functions (EF), and socio-emotional difficulties possibly associated with deficits in Theory of Mind (ToM). In this study, we probed the relationship between ToM and EF in children with ADHD and controls.

Methods. Ten children with ADHD and 10 matched healthy control children participated in this study. Assessment and differential diagnosis were carried out using the Diagnostic and Statistical Manual for mental disorders (DSM IV) criteria. All children were administered a standard neuropsychological battery (including EF and ToM tasks). ToM functions were evaluated using 2 tasks ("Faux pas" and "Eyes" tasks) which demand different levels of executive involvement.

Results. Concerning EF, ADHD children showed impaired performance as compared to controls in WM (Forward and Backward Digit Span $t(16)=4.13$, $p=0.001$; $t(16)=2.15$, $p=0.047$), inhibition (Numerical Stroop: all $t(17) > -2.56$, $ps<.05$) and flexibility (Revised Wisconsin Card Sorting test $t(17)=-2.09$, $p=0.052$; Flexibility subtest: all $t(17) > -2.15$, $ps<.05$; Semantic and Phonemic Fluency: $F(1,15)=5.61$, $p=0.03$ and $F(1,15)=4.9$, $p=0.04$). Concerning ToM, ADHD children performed more poorly than controls for the Faux pas ($F(1,19)=4.907$, $p=0.04$) and the Eyes ($F(1,19)=8.19$, $p=0.01$) tasks. Pearson's correlational analyses were computed between ToM and EF in our 2 groups separately. In the control group, the Faux pas task is correlated with tasks involving WM and inhibition, and the Eyes task with flexibility and inhibition tasks (all $r > +/- 0.67$, $ps<.05$). In the ADHD group, the Faux pas task is correlated with tasks involving WM and flexibility, and the Eyes task with attentional, flexibility and inhibition tasks (all $r > +/- 0.63$, $ps<.05$). Finally, linear regression analyses in the ADHD population indicated that ToM tasks were best predicted by flexibility, WM and attentional components (all $t >+/-2.68$, $ps<.05$).

Conclusion. Results yielded evidence for deficits both in EF and ToM in ADHD children, and significant correlations between performance on EF and ToM tasks. Also, performance on EF partially explained ToM deficits in ADHD. Altogether our results corroborate the hypothesis of ToM alterations in children with ADHD, possibly linked with EF deficits. These deficits may contribute to the social difficulties experienced by some ADHD children.

Influence of microarousals on subjective sleep quality

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These days more and more people pay attention to their sleep and its quality. Some of them feel poorly after the sleep even though they had slept all the night. Recent findings showed, that subjective satisfaction after the sleep is not dependent on the sleep length (Zamit, 1999). Amount of delta sleep is not the main factor for subjective sense of rest after the sleep (*Roth ir Roehrs, 2003*); There are evidences, that even people with sufficient sleep length, good blood oxygenation feel poorly after the sleep (Martin et al., 1997);More and more attention recently is paid for the sleep integrity and sleep fragmentation, which is characteristic for a primary insomnia (Terzano et al., 2003) and could have effect on the sleep restorative function.

Purpose of our research is to analyze sleep fragmentation in men and women groups by scoring cortical microarousals(MA) in all sleep stages and to evaluate microarousals correlation with subjective sense of rest after the sleep, regardless of the type of insomnia.

Goals of our research were:
– to estimate sleep quality by means of objective - microarousal indexes (MAI) - and subjective - Pitsburgh questionnaires (PSQI) - data;
– to evaluate if there is a correlation between MAI and patients' age and between PSQI and patients' age;
– to evaluate if there is a correlation between MAI and PSQI, id est objective and subjective data;
– to evaluate whether there are any gender differences between objective and subjective data.

Methods: Polysomnography(PSG) and Pitsburgh sleep quality index(PSQI) . PSG was the source of our objective data – that is MAI, and the Pitsburgh sleep quality questionnaires were the source of our subjective data – that is PSQI.

Results:
– PSQI values are significantly lower (p = 0,008) in men than in women group whereas MAI values are not significantly different in these groups;
– correlation between MAI and patients' age is moderate in men group (R = 0,49; p =0,03) and negative very weak in women group (R = -0,24; p = 0,3);
– correlation between PSQI and patients' age in men group is moderate (R = 0,42; p=0,07) and in women group it is very weak (R = 0,25; p = 0,28);
– correlation between MAI and PSQI in men group is moderate (R = 0,41; p = 0,08)
– and in women group there is no such correlation at all (R = 0,098; p = 0,68);

Conclusion: only from cortical MAI we could not judge about the patients subjective sleep quality.

Sleep-related problems of Parkinson's disease in Lithuania

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Background and objectives. According to the literature as many as 98% of patients with Parkinson's disease (PD) may suffer at some time from nocturnal symptoms that can disturb their sleep. Sleep-related problems specific to PD can seriously compromise patients' quality of life, lead to impaired functioning in daily activities and cause huge costs related to the healthcare. However, it is only recently that sleep disturbances related to PD have received much diagnostic and therapeutic attention worldwide. In Lithuania these problems are still under-recognized and under-treated.
The aim of the study is to define the epidemiology, characteristics and aetiology of nocturnal symptoms and sleep disorders in patients with Parkinson's disease in Lithuania and evaluate the available methods for their diagnosis and management.

Methods. The participants of the study are patients with Parkinson's disease reffered to Parkinson's disease Center in Vilnius. Demographic data, disease characteristics, treatment data are collected from case histories. The patients are inquired about their sleep associated complaints, sleep habits.

Results. The study is still ongoing.

Conclusions. Sleep disorders associated with PD are a common and under-recognized problem. The assessment of sleep should be part of the routine evaluation of patients with PD.

Switching Attention to Insomnia: the Role of Objective Sleep Duration

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Objectives. Chronic insomnia with objective short sleep duration is associated with hyperactivity of the hypothalamic-pituitary-adrenal axis and with significant medical morbidity (e.g. hypertension). Here, we report the results of 4 studies aimed at exploring the joint effects of chronic insomnia and objective sleep duration on neuropsychological functioning, long-term development of depression, personality, and sleep misperception in a general population random sample of 1741 individuals (Penn State Sleep Cohort).

Methods. "Insomnia" was defined as a complaint of insomnia with a duration of > 1 year and the absence of sleep-disordered breathing (SDB). We classified polysomnographic (PSG) sleep duration into two categories: > 6 hours of sleep and < 6 hours of sleep. We controlled for age, race, gender, education, BMI, mental, and physical health problems in all multivariate ANOVA and regression analyses.

Results. Compared to controls, the insomnia with < 6 hour sleep duration group showed deficits in tasks of processing speed, short-term memory, and switching attention, and a higher risk to develop depression at 5 years follow-up, which was independent of their personality profile. In contrast, the insomnia with > 6 hour sleep duration group did not show significant neurocognitive deficits and their risk of developing depression was mediated by their anxious-ruminative psychological profile; however, this group significantly complained of non-restorative sleep and presented a gross underestimation of sleep time.

Conclusions. Insomnia with objective normal sleep duration is related to sleep misperception, non-restorative sleep, and anxious-ruminative traits. Insomnia with objective short sleep duration is associated with a psychological profile typical of medical outpatients, which does not explain their higher risk for developing depression; also, this group presents deficits in the "executive control of attention", a higher cognitive function that involves the prefrontal cortex. Thus, objective sleep duration in chronic insomnia may be a reliable index of the biological severity of the disorder.

Positive effects of Red Bull® Energy Drink on driving performance during prolonged driving

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Objectives. Prolonged highway driving can be affected by sleepiness. During driving, performance progressively gets worse. It is therefore advised to have a 15-minute break after every two hours of continuous highway driving. The purpose of this study was to examine the effects of Red Bull® Energy Drink versus placebo during this break on highway driving performance.

Methods. 24 healthy volunteers participated in this double-blind placebo controlled crossover study. After 2 hours of driving in the STISIM driving simulator subjects had a 15-minute break, in which they consumed Red Bull® Energy Drink (250 ml) or placebo (Red Bull® Energy Drink without the functional ingredients caffeine, taurine, glucuronolactone, and B vitamins) before driving for two additional hours. A third condition comprised 4 hours of uninterrupted driving. Primary parameter of the highway driving simulator test was the Standard Deviation of Lateral Position (SDLP), i.e. the weaving of the car. Secondary parameters included the standard deviation of Speed, subjective driving quality, mental effort to perform the test, and subjective sleepiness.

Results. In the first two hours, no significant differences between the treatments were observed on any parameter. Relative to placebo, Red Bull® Energy Drink significantly improved driving: SDLP values were significantly reduced during the 3rd ($p<0.046$) and 4th hour of driving ($p<0.011$). During the 3rd hours, Red Bull® Energy Drink significantly reduced the standard deviation of Speed ($p<0.004$). In line, for the 3rd hour of driving after consumption of Red Bull® Energy Drink subjects reported significantly improved driving quality ($p<0.0001$) and reduced mental effort to perform the test ($p<0.024$). During both the 3rd and 4th hour of driving, subjective sleepiness was significantly less pronounced after Red Bull® Energy Drink when compared to placebo ($p<0.001$ and $p<0.009$, respectively). Relative to prolonged driving, the effects of Red Bull® Energy Drink were significant for each parameter during both the 3rd and 4th hour of driving, except for mental effort during the 4th hour of driving.

Conclusion. Red Bull® Energy Drink significantly improves driving performance during prolonged driving.

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The effects of neurofeedback on memory performance and sleep

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Objectives. The individually-dominating alpha frequency, manifested by a peak in the EEG spectrum, has been shown to correlate with memory performance. In various neurological diseases linked to memory impairments (e.g. Alzheimer´s disease, stroke, and traumatic brain injury), a reduction in the individual alpha frequency was found. Neurofeedback provides the possibility to voluntarily influence and modify brain activity.
The present study investigated the effects of induced band power shifts on declarative memory performance as well as on sleep quality of a 90-min midday nap.

Methods. Sixty healthy young subjects (30 male, 30 female; mean age = 23.58 years, SD = 3.18) were randomly assigned (double-blind study design) to either (i) a neurofeedback protocol (experimental group; n=30) or (ii) a sham-feedback protocol (control group, n=30). Each session was split in 6 × 3 minutes sessions with in-between breaks of 30 seconds. Subjects were trained to enhance upper alpha activity (10-12 Hz; while keeping lower alpha power as small as possible) during 10 conditioning session within the study period of 14 days. All participants got equal instructions; in the experimental group subjects were trained to increase their individual upper alpha activity by receiving continuous visual feedback about the progress of their upper alpha power, whereas in the control group the feedback was applied independent of the upper alpha frequency, in a random order. Before and after the training conditions subjects were tested on a paired-associate word list. Semantically unrelated word pairs (n = 160) were presented sequentially on a monitor. Retrieval was done directly after learning and after a consolidation period of 90 minutes during which subjects had the opportunity to take a midday nap (2 pm – 3:30 pm). Performance of experimental and control group were compared, and influences of neurofeedback on memory consolidation during sleep were analyzed.

Results. The following main results were found: (i) Upper alpha activity increased significantly between the training sessions 1 to 10 in the experimental group ($F = 4.472$, $p = 0.003$). (ii) Total wake time decreased significantly after neurofeedback training in the experimental condition ($T = 2.438$; $p = 0.021$). (iii) Performance increased significantly in the experimental condition ($\chi^2 = 17.637$; $p = 0.001$).

Conclusion. Neurofeedback training enhances sleep quality as well as memory performance.

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Sleep and temperature in Alzheimer's disease and healthy controls

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Sleep in old age is lighter, shorter, and more fragmented than in young. In Alzheimer's disease (AD) these characteristics become more pronounced. A disturbed rest-activity rhythm in severe dementia may contribute to the risk of institutionalization. Alterations in the suprachiasmatic nucleus (SCN) probably contribute to this disturbance, especially in AD. This leads to the assumption that when the sleep-wake rhythm alters, changes will be evident in other circadian rhythms as well, such as temperature rhythm, which is strongly coupled to the sleep-wake rhythm. The aim of the present study was to examine the relationship of the 24-hour skin temperature rhythm to actigraphically estimated and subjectively reported sleep in AD and healthy controls.
Participants were mild AD patients (37m/15f, 70.4±3.2 years old) and healthy age matched controls (15m/9f, 67.2±7.7 years old). All subjects wore an actiwatch for 2 weeks to estimate sleep parameters. A pressure pad placed on the mattress and connected to a logger with integrated light sensor was used to record bed times and lights out times. During the first 24 hours, subjects also wore 9 miniature iButton temperature data loggers to measure distal and proximal skin temperature. Daytime and night time averages were calculated over the periods that subjects were out of bed and in bed respectively. Questionnaires used to obtain subjective measures were the Athens Insomnia Scale, the Pittsburg Sleep Quality Inventory and the Sleep Disorders Questionnaire (SDQ). Spearman's correlations were calculated between parameters and independent sample t-tests used to compare the two groups.
Preliminary data show a significant higher daytime proximal temperature in AD ($p = 0.00$). In controls, proximal night time temperature was negatively correlated to wake after sleep onset (WASO, rho=-.49, p=0.01) and to the average duration of nocturnal awakenings (rho=-.47, p=0.02). In AD, distal night time temperature correlated negatively with WASO (rho=-33, p=0.02), percentage wake (rho=-31, p=0.03) and the average duration of nocturnal awakenings (rho=-.41, p=0.00). A positive correlation was found with sleep efficiency (rho=-31, p=0.03). The excessive daytime sleepiness subscale of the SDQ correlated to daytime proximal temperature in both controls (rho=.40, p=0.05) and in AD (rho=.35, p=0.01). The data indicate that proximal skin temperature is intricately linked to the sleep and vigilance parameters, and that its regulation is disturbed in AD.
Furthermore, a high proximal skin temperature is essential in maintaining sleep throughout the night. It seems that due to the disturbed proximal rhythm in AD, distal temperatures become more present in the maintenance of undisturbed sleep.

Differences in melatonin therapy response in elderly patients with various ages at the onset of insomnia

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Introduction. Biological aging is often associated with insomnia. The link among melatonin levels, pineal function, and insomnia is strengthen by epidemiologic and chronobiological evidence.

Purpose. We examined whether sleep disorders in old age responds particularly to the treatment with melatonin, in comparison with the adult patients with insomnia and whether melatonin has an influence on age related insomnia, in elderly people with late onset of insomnia.

Method. We ran an open label study on 64 subjects. None suffered from depression, dementia, sleep apnea or restless legs syndrome. Data such age, sex, and the age at the onset of insomnia were collected. The study population comprised two groups: one group with patients with insomnia whose ages were over 65 years (31 subjects) and the other group with young adults, with ages between 20 and 39 years (33 subjects). We have divided the elderly group in two subgroups: the first with a long history of insomnia (16 subjects with the onset of insomnia before reaching 50 years) and the second with a late onset of insomnia (after 50 years of age, 15 subjects).
The Athens Insomnia Scale (AIS 5) 5 item version was administered to the two groups before and after the treatment with melatonin. The AIS is a self assessment psychometric instrument designed for evaluating sleep modifications based on the ICD-10 criteria. It consists of five items referring to: sleep induction, awakenings during the night, final awakening, total sleep duration and sleep quality.
The patients took a single daily dose of 5 mg of melatonin 30 minutes before bedtime. Using the AIS-5, we have assessed sleep before treatment and after 4 weeks of treatment. SPSS version 11 was used for statistical analysis

Results. After 4 weeks of melatonin therapy (5 mg/ day), the sleep quality in elderly insomniacs improved more than the sleep quality of young adults (median AIS score: 4 versus 8; $p < 0.018$).
The melatonin had a more positive influence on the sleep of the group with late onset of insomnia, but without a statistical significant difference from the elderly subgroup with the onset of insomnia before reaching 50 years.

Conclusions. Comparison of the two groups suggests that melatonin is more effective in elderly insomniacs. Melatonin replacement seems to be beneficial especially in elderly people with late onset of insomnia. This could be a future trend in the psychopharmacology of the sleep in elderly, instead of chronically use of benzodiazepines.

Spatial cognition of animals and humans based on abstract spatial stimuli: Model for higher cognitive functions

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An ability to create and store an internal representation of space is crucial for most animal species including humans.
We developed a set of cognitive tests to study an ability of animals not only to encode their own position but also to encode the space per se and to perform complex cognitive functions (e.g. mental rotation).
In the first task rats were placed in the Skinner box facing a computer screen. They observe moving objects or objects in particular positions displayed on a screen. The rats were rewarded for lever pressing when the objects on the screen were in a particular spatial configuration. This allows us to assess an ability of rats to recognize position of distant objects.
In the second task the subjects should use abstract visual stimuli to orient in a real environment. We showed earlier that animals including rats and macaques could make spatial choices in the real space using abstract visual stimuli presented on a computer screen.
The animals were in a box allowing them to watch the stimuli presented on a screen. They choose correct position in a „real response space" according to these stimuli. The response space for monkeys was a touch screen or a touch panel placed separately beside the monitor. The panel was a transparent board with nine touch-holes in a 3 x 3 array registering a touch. The rats responded by nose-poking in one of four nosing-holes in a transparent front wall of the box.
Initially, we used as stimuli symbolic representations of the response space. Rectangle represented the panel and a circle shown in one of the nine positions in the rectangle marked the position of the rewarded hole. Later, we transformed the stimuli: they were rotated or with changed Euclidean features (lengths of sides, angles).
We studied the ability of animals to encode abstract spatial information provided in one spatial frame (computer screen) and to perform spatial decisions in another spatial frame (touch panel separated from the screen).
Using of the computer screen to present the stimuli allows us to study spatial cognition in wide range of tasks with minimization of locomotor component.

Evaluation of p wave dispersion, qt dispersion and p wave amplitude in patients with obstructive sleep apnea syndrome

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Objective. The purpose of the present study is to investigate the risk of atrial and ventriculer tachyarrhythmias by calculating P wave dispersion(Pd) and QT dispersion(QTc) which is reported to predict the risk of atrial and ventriculer tachyarrhythmias, and to evaluate the risk of right artial dilatation by calculating P wave amplitude(Pda) in patients with obstructive sleep apnea syndrome(OSAS).

Method. Patients who had applied to our sleep laboratory between January 1 2008 to July 1 2008, enrolled the study. 225 patients (84 female, 141 male) who met the inclusion criteria, were included in the study. Blood tests of the patients were analysed. Additionally, all the patients underwent electrocardiography. Pd, Pda QTc ve corrected QT dispersion (QTcd) calculated on a 12 lead surface ECG. Differences between patients and control group were evaluated.

Results. After polysomnographic analysis , 56 cases with AHI<5 were included as the control group and 161 patients with AHI≥5 were included as the patient group. The mean age of the cases was 48.3±8.9. There was no statistically significant differences between patient and control group with regard to QT min, QT max, QTd ve QTcd parametres ($p>0.05$). Althought QTc was higher than normal range in patient group, the differences was not significant compared to control group ($p>0.05$). Though P max, P min and Pd were higher in patients group compared to control group, the differences was not statistically significant. However, P wave amplitude was significantly higher in the patient group than in the control group ($p=0.02$).

Conclusion. Pd and QTc/QTcd do not seem to be suitable parametres to evaluate the risk of atrial and ventriculer tachyarrhythmias in patients with OSAS. However, higher P values in OSAS patients might point at the increased risk of right atrial dilatation. Further studies are required to clarify this subject.

Overt replay of a recently learned motor sequence during human slow-wave sleep in sleepwalkers

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Objectives. Mounting evidence suggests that sleep consolidates memory, possibly because newly acquired information is replayed during sleep. Support for this hypothesis comes from animal local field recordings (neuronal replay) and, indirectly, from functional brain imaging (regional reactivation) in humans. There is however a challenging debate concerning sleep-associated regional reactivation in human: do local increases in neural activity correspond to a true, temporally-structured replay of the recent patterned neural activity, or does this merely reflect local homeostatic processes?

Methods. We used two sleep disorders, sleepwalking (occurring during slow-wave sleep) and rapid eye movement sleep behavior disorder, in which patients overtly act out parts of their sleep mentations, as models to test whether humans would replay during sleep a recently learned sequence involving large arm movements during sleep. Twenty patients with RBD, nineteen sleepwalkers and eighteen healthy controls were trained on a variant of the serial reaction time task that required ample hand and arm movements, thus forming a specific ‘choreography’.

Results. Subjects with both disorders showed improved performance in the learned sequence after sleep. One sleepwalker clearly acted out a fragment of the motor sequence during slow-wave sleep.

Conclusion. This study supports a role for cognitive (and associated neural) replay in overnight consolidation of complex motor skills.

Double knockout mice lacking histamine and orexins: a full model of narcolepsy for physiopathological and therapeutic studies

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Objectives. Using knockout (KO) mice lacking histamine (HA) or orexins (Ox), we have previously shown that HA and Ox exert a distinct but complementary control of wakefulness(W): the amine, mainly responsible for the qualitative cognitive aspect, its deficit leads to somnolence, whereas Ox, more involved in locomotion and behavioural activation, their defect causes narcoleptic attacks (direct onsets of paradoxical sleep from W, Anaclet et al., J.Neurosci.2009). To assess their synergy in W control under physiopathological conditions, we have generated a double KO mouse strain which lacks of both HA and Ox (HO-/-) and which shows all major narcoleptic phenotypes: cataplectic (sudden loss of muscle tone during W) and narcoleptic attacks, somnolence and hypersomnia (Anaclet et al., Sleep(suppl)2010). This mouse strain is therefore a full model of narcolepsy. This study further characterized its pharmacological responses.

Methods. Adult male HO-/-mice and their wild-type (WT) littermates (n=16 pairs) were simultaneously investigated using multidisciplinary approaches, e.g., PCR genotyping for genes of Ox and the HA-synthesizing enzyme, polygraphic sleep-wake recording, cortical EEG spectral analysis and pharmacological dosing.

Results. As previously shown (Anaclet et al.,2010), HO-/-mice presented all phenotypes of the single KO mice lacking HA or Ox, notably narcoleptic attacks during darkness and an aggravated hypersomnia at lights-off, during darkness and over 24. We examined the effects of pharmacological dosing on these phenotypes and found that 1) Modafinil (64 mg/kg, p.o.), a clinically used W-promoting agent, enhanced W during both lightness and darkness; 2) HA H3-receptor inverse agonists enhanced markedly W and cortical fast rhythms in WT mice, but had no effect in HO-/-mice, indicating absence of functional HA; 3) orexin-A (3 µg, i.c.v.) increased W and suppressed narcoleptic attacks in HO-/-mice; 4) scopolamine, a muscarinic antagonist (0.25-0.5 mg/kg i.p.) induced no visible effects in WT but increased cortical slow activity and decreased W, paradoxical sleep and narcoleptic attacks in HO-/- mice.

Conclusion. The hypersomnia of HO-/-mice indicates gravely impaired arousal mechanisms in spite of possible up-regulation of the waking systems other than HA and Ox, such as the cholinergic system. This murine model appears appropriate for pathophysiological and therapeutic studies of narcolepsy.

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WAY-100635 attenuates phrenic long term facilitation in rats

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Objectives. To investigate the effect of 5-HT_{1A} receptor antagonist WAY-100635 on the phrenic long-term facilitation (pLTF) in rats. We hypothesized that there would be a significant attenuation of pLTF in the group of animals treated with WAY-100635 in comparison with control group of animals.

Methods. Fourteen adult, male, urethane anesthetized, vagotomized, paralyzed, and mechanically ventilated Sprague-Dawley rats (7 per group), were exposed to the acute intermittent hypoxia (AIH) protocol. Experimental group of animals received an intravenous injection of WAY-100635 before the onset of the first hypoxic stimulus. Peak phrenic nerve amplitude (PNA), burst frequency (f), and breathing rhythm parameters (Ti, Te, Ttot) were analyzed during the first hypoxia, as well as at 15 (T15), 30 (T30), and 60 minutes (T60) after the end of the last hypoxic episode, and compared to the baseline values.

Results. In control group of animals, there was a significant increase of PNA (58.7 ± 3.3%, $p<0.001$) at T60. PNA of animals treated with WAY-100635 showed a slight decrease at T60 by 15.1 ± 1.7%.

Conclusion. The pLTF, elicited by AIH, was induced in the control group of animals. On the contrary, administration of WAY-100635 significantly attenuated pLTF in rats.

Keywords: respiration, phrenic nerve, intermittent hypoxia, rats, neuronal plasticity, serotonin

A nap - as good as a night?

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In succession of a study by Mednick et al. (2003) showing that short periods of sleep can be as beneficial for memory consolidation as longer periods, many studies investigated the influence of naps on memory consolidation. A closer look at nap literature, however, reveals that results are not consistent. Some nap studies on declarative as well as procedural memory reveal a nap effect whereas others do not. When looking at declarative memory, the ambiguity in results could be due to differences in learning materials and experimenttal designs.
Experiments differ, e.g., with regard to material (words, pictures), mode of presentation (oral, visual), and manner of recall (free, cued, recognition). From the variety of results, no clear picture emerges. In a series of nap studies, we tried to find reliable effects of nap periods on memory performance.
In a first study, subjects were presented semantically unrelated word pairs and performed an immediate recognition test. After either 60 min of napping or staying awake, subjects learned an interference list. Participants then underwent a recall (50% cued, 50% recognition) of the original list. Results showed no significant differences between the wake and the sleep group.
In the second study, subjects were presented semantically unrelated word pairs. They then either went to bed for 90 minutes or stayed awake. After a delay of 5 hours, half of the word pairs were tested before and half of the word pairs were tested after subjects learned an interference list. No sleep effects were found, either with or without intervening interference.
The third study investigated the effect of nap sleep on both procedural and declarative memory. Subjects learned related and unrelated word pairs and they practiced a finger sequence tapping task. They then had a nap for 120 minutes or stayed awake. 6 hours later, recall was tested. Sleep effects were found for procedural, but not for the declarative memory task.
Together, from our view of recent literature and our own experiments, we doubt whether there is a general effect of short sleep periods (naps) on declarative memory consolidation. This effect might, however, appear under special circumstances, which remain to be elucidated. On the other hand, we could replicate the effect of naps on procedural memory in the finger sequence tapping task.

Correlation Between Cyclic Alternating Pattern Parameters And Subjective Daytime Sleepiness Scores

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Objectives. To analyze the relationship between objective sleep variables and subjective complaints of excessive daytime sleepiness (EDS) in patients with obstructive sleep apnea syndrome (OSAS).

Methods. Twenty-nine randomly selected male subjects with different levels of subjective daytime sleepiness, measured with the Epworth Sleepiness Scale (median score 8 +/- 4.5), referred to our sleep laboratory, were included in the study. Each participant underwent a polysomnographic study and the parameters for sleep macrostructure, sleep microstructure and breathing disturbances were recorded and scored. Nonparametric Spearman rank correlation analysis was performed to clarify the relationship between objective sleep variables and subjective complaints of EDS.

Results. Epworth sleepiness score (ES) revealed fairly high correlations with cyclic alternating pattern (CAP) time ($r_s=0.66$; $p<0.001$); CAP rate ($r_s=0.62$; $p<0.001$), classical arousal index (ArI) ($r_s=0.60$; $p<0.001$) and respiratory disturbance index (RDI) ($r_s=0.65$; $p<0.001$). Weaker correlations were observed with CAP-A3 index ($r_s=0.42$; $p<0.05$); CAP-A2 index ($r_s=0.41$; $p<0.05$) and A1/A2 ratio ($r_s=-0.55$; $p<0.05$). Other CAP parameters (A1 index, A1 mean duration, A2 mean duration, A3 mean duration, CAP-B mean duration and A1/A3 ratio) failed to yield significant results. The analysis of sleep macrostructure (percentages of sleep stages, latencies of N2, N3 and REM stages, total number of stage shifts and number of stage shifts per hour) also failed to show any statistically significant correlations with ES.

Conclusion. Our results suggest that the increased sleep instability, assessed by CAP-time and CAP-rate, as well as the classical ArI and RDI, all have a relatively high predictive value for subjective complaints of daytime sleepiness. In contrast, changes in sleep architecture, typical of OSAS, are of no importance for developing EDS. Our results are consistent with previous findings that analysis of sleep microstructure is superior to analysis of sleep macrostructure in respect to daytime complaints.

Task-induced neuronal network connectivity reappears during sleep in humans

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Objectives. Research has shown that sleep helps consolidate recently acquired memory. One hypothesis suggests that neuronal connections that have been activated during a task are reactivated during subsequent sleep.
In humans, local reactivation during sleep of recently activated cortical areas has been demonstrated, but until now there is no evidence of reappearance of connections between previously coupled distant cortical areas. The aim of the present experiment was to test whether task-induced oscillatory behavior of long-range cortico-cortical connections selectively reappears during subsequent sleep.

Methods. Magnetoencephalographic (MEG) data were acquired from eight participants during performance of two tasks, each on a separate day in balanced order. A mirror tracing task and a face-name association task were chosen because they engage different neuronal networks as they involve procedural and declarative learning, respectively. After each task, participants were invited to take a 90 minute nap, equivalent to the duration of a sleep cycle.
Connectivity was assessed by correlating fluctuations in power between sensors in the beta frequency band for the tasks and in the slow oscillation band, delta band and spindle frequency band for sleep. We used the nonparametric permutation statistics to test whether sensor pairs that were more correlated in one task than in the other were also more correlated during the corresponding sleep periods.

Results. Sensor pairs that showed high beta-power correlations selectively during the procedural learning task were found to pair again, above chance level, in the delta band during subsequent sleep ($p = .004$).
This reactivation of connectivity was not found in the slow-oscillation or spindle band. Recoupling could not be demonstrated for the task-induced beta-power correlations in the declarative learning task ($p = .60$). The connections that reappeared during sleep following the procedural learning task are located over the pre-motor and the parietal cortices, indicating process-specificity.

Conclusion. Connectivity between brain regions induced by a motor learning task, as identified by beta-power correlations between sensors, reappeared during subsequent sleep in the delta band. The reconnected areas are implicated in motor control and visuospatial processing.
To our knowledge, our findings are the first to indicate that reappearance of oscillatory coupling in task-relevant neuronal networks occurs in humans.

Ventilation limitation during exercise in men with obstructive sleep apnoea

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Some obese people develop ventilation limitation (VL) during exercise and the predisposing factors are not obvious. A lot of obstructive sleep apnoea (OSA) patients are overweight. VL in OSA patients has not been investigated.

The objective of this study was to assess the presence of VL during exercise testing and to identify the factors possibly related to it in men with OSA.

Methods. To avoid gender differences only men were included in this study. OSA was confirmed by the whole-night polysomnography, when apnoea/hypopnoea index (AHI) was >5/h. Exercise testing consisted of resting period, 2 minutes warm-up and increasing work rate by 40 W every 2 minutes. All the tests were terminated at the point of symptom limitation. The presence or absence of VL was estimated by evaluating expiratory flow limitation by measuring the tidal breath during exercise that encroached on the maximal flow envelope, registered during resting period. Borg scale was used to evaluate exertional dyspnoea and legs discomfort. Height and weight was measured and body mass index (BMI) was calculated. Sleepiness was evaluated by the Epworth Sleepiness Scale. All the subjects were divided into two groups according to the presence or absence of VL.

Results. Sixteen men were tested. All of them had normal lung function proved by spirometry (FEV1 97.8+/- 9.7 % predicted). Nine of sixteen patients developed VL. There was no statistical difference between age and BMI in the groups with and without VL (mean +/- SD respectively: age 42+/-12 and 41+/-10 years, BMI 38.4+/-6.9 and 31.8+/-7.0 kg/m^2, p>0.05). AHI was higher in the group with VL (65.9+/-26.8/h) than in the group without VL (19.4+/-10.6/h) (p=0.003, Mann-Whitney U test). There was no statistical difference between peak oxygen consumption (VO2), Borg and Epworth scale parameters in those two groups.

Conclusions. Men that developed VL during exercise had more severe OSA, proved by higher AHI, but their BMI did not differ. Further investigations should be performed to explain these findings.

Electrophysiological correlates of processing aversive experiences in an animal model

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Objectives. The amygdalo-hippocampal circuit plays an important role in the formation and processing of memories of an aversive event. As it has been shown in mice (Narayanan et al., 2007a; Narayanan et al., 2007b; Pape et al., 2005; Seidenbecher et al., 2003), rhythmically synchronized activity at the theta frequency band increased between the lateral amygdala (LA) and the CA1 region of the hippocampus after fear conditioning and became significant during confrontation with conditioned fear stimuli and expression of fear behavior (freezing). The aim of the present study is to evaluate if similar oscillatory patterns can also be observed in animals that experienced a traumatic event.

Methods. Using our animal model for the Posttraumatic Stress Disorder in mice (PTSD; Siegmund and Wotjak, 2007; Siegmund and Wotjak, 2006) the animals will be exposed to a single electrical footshock at a strength of 1.5 mA as the analogy for a traumatic event. Simultaneous chronic recordings of deep electrodes in the LA and CA1 in combination with chronic electroencephalography (EEG) and electromyography (EMG) will be performed in freely moving mice.

Results. Combining the recordings of data from EEG/EMG and deep electrodes within LA and CA1 will give additional information about first, communication between the hippocampus, the amygdala and the cortical areas on the procession of a traumatic event, and second, about the sleep stages in which potential communication occurs. Furthermore, the electrophysiological recordings during the re-exposure of the animal to a part of the traumatic context (e.g. the odor or the environment) will be used for measuring potential synchronous activity as an indicator of the re-experiencing symptoms as they are reported for PTSD patients.

Conclusions. Based on the results of this up-coming study, new insights into the disturbed neuronal processing of an aversive event in PTSD patients can be achieved. Further experiments using extinction training or pharmacological interference could shed light on the neuronal circuits that underlie both behavioural and pharmacological therapy in patients with anxiety disorders like PTSD.

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Sleep, mood and emotional processing

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Objectives. To investigate the effect of negative mood induction and total sleep deprivation on mood, emotional processing and sleep in people with and without a positive family history of affective disorders. Initially the protocol is being piloted in people without a positive family history.

Methods. The effect of an analogue depressing experience is being compared between sleep deprived (SD) and non sleep deprived (nSD) participants. None of the participants have psychiatric or sleep problems and all undergo circadian profiling prior to the experiment, using actigraphy, melatonin and cortisol assaying. The experiment, carried out in our sleep facility, involves the participants watching a depressing film followed by a period of sleep deprivation or normal sleep. Also the participants experience a stressful event using the remote associates' task, and polysomnography.

Results. This study is ongoing (n=12). The two groups are matched for age, daily caffeine intake, morningness/eveningness, profile of mood state and Eysenck personality questionnaire scores. No differences have been found for any actigraphy parameters. The study film has been found to cause a significant change in mood for all participants ($p<=0.05$): self reported sad, horrified and tense moods increase while happy mood decreases using a visual analogue scale; anxiety levels increase after watching the film, using the state anxiety scale. We also find that the SD group has a lower positive and higher negative mood after 24 hours of sleep deprivation using the positive and negative affect scale. The stressful event causes a significant increase in sad, horrified, hopeless and awkward moods as well as anxiety levels, while self reported calm and happy mood significantly decreased ($p<=0.05$). To date, no difference has been found between the groups in terms of response to the stressful event and number of spontaneous intrusive memories relating to the film being reported.

Conclusion. We have shown that this protocol is working in terms of expected changes in mood due to the film and sleep deprivation. Also the production of intrusive memories is consistent with previous studies (Holmes et al 04; *J Exp Psychol Gen*). Contrary to what we expected the SD group did not respond differently to the stressful event than the nSD group. This could be explained by the low study numbers so far. A further explanation might be that the SD group shows a reduced emotional reactivity.

The role of psychological beliefs about sleep and insomnia and insomnia-related behavior in subjective and objective sleep

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Background. Illness representation and consequent patients' behaviors are suggested to be factors perpetuating illness (Leventhal, 2003). In insomnia self-focused attention and self-monitoring provoke self-limiting behavior and passivity in patients which perpetuate insomnia symptoms (Harvey, 2005). However, there are few studies of positive psychological buffers against insomnia and of their influence on patients' behavior and insomnia symptoms.

Aim. To investigate the role of different types cognitive beliefs about sleep and insomnia and coping behavior in primary insomnia perpetuation.

Methods. 83 primary insomnia patients and 105 good sleepers filled Hospital Scale of Anxiety and Depression (Hamilton), Insomnia Severity Inventory, Dysfunctional Beliefs About Sleep Scale (Morin), Glasgow Content of Thoughts Inventory (Harvey & Espie), Beliefs About Sleep and Insomnia Checklists (Rasskazova). Polysomnography was recorded in 63 insomniacs and 10 good sleepers (including EEG, EMG, EOG).

Results. Dysfunctional beliefs about sleep (Morin, 1993) are related to increase in the second stage of slow-wave sleep and worsening of subjective sleep. Ruminations before sleep (Harvey, Espie, 2004) correlate with decrease in deep-sleep slow waves and subjective sleep index.
Patients were divided according to their behavior during the day (self-restrictive behavior, passivity, sleep rituals, daytime insomnia-related coping activity). Insomnia-related passivity and especially self-restrictive behavior are correlated with significant decrease in delta-sleep and insomnia duration, whereas patients with sleep rituals have better subjective sleep but experience more anxiety.
Beliefs about sleep and insomnia and insomnia-related behavior independently predict subjective and objective sleep in patients (RMSEA=0.05, CFI=0.94).

Conclusion. Patients' activity in insomnia mediates the relationship between illness representation and subjective and objective severity of insomnia. Patients' beliefs and activity are related to insomnia perpetuation.

Sleep-disordered breathing and paroxysmal nocturnal behaviours in extrapyramidal syndromes: which relationship?

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Objectives. Patients with idiopathic Parkinson's disease (PD) or other extrapyramidal syndromes (non-PD EPS) often experience disrupted nocturnal sleep of multifactorial origin. Respiratory disorders in sleep and complex paroxysmal nocturnal motor behavioural disorders (CPNBs) are both described in these populations. CPNBs were shown to include REM sleep behaviour disorder (RBD) and NREM arousal-related paroxysmal episodes. This study is aimed at investigating the relationship between SDB and CPNBs.

Methods. We studied a population of around 200 subjects affected with PD or non-PD EPS (the latter including dementia with Lewy bodies, multiple system atrophy, progressive supranuclear palsy or other unclassified parkinsonisms), with and without anamnestic report of respiratory disturbances during sleep or CPNBs, referred to the Sleep Laboratory by the Motor Disorders Unit of our Institute in a four-year period. All patients underwent a full-night video-polysomnographic recording.

Results. About the 30% of PD and 40% of non-PD extrapyramidal patients had obstructive sleep apnoeas (p=ns). No significant difference in prevalence of CPNBs was observed between PD and non-PD EPS patients. In PD patients, subclinical or full-blown RBD episodes were captured in about the 79% of cases, NREM parasomnias (consisting of either RBD-like manifestations or complex motor behaviours including wandering, disperceptive phenomena or aggressive and sex behaviours) in 18% and both in 3%. In EPS patients, RBD episodes were captured in 69% of cases, NREM parasomnias in 18% and both in 13%.
CPNBs were related to obstructive apnoea in about 40% of PD patients and 20% of non-PD EPS patients (p=ns). In PD patients, 8% of CPNBs occurred in REM sleep, 20% were NREM parasomnias and 100% of overlapping episodes were related to an apnoea-associated arousal (p=.0008).
In non-PD EPS patients, this relation was present in about 30% of NREM parasomnias, 20% of overlapping episodes but in no case of CPNBS occurring in REM sleep (p=.0013).

Conclusion. Obstructive sleep apnoeas were found in a not negligible percentage of extrapyramidal patients.
A small proportion of CPNBs seems to have a strict relationship with apnoea-related arousals.
The presence of sleep apnoea is more likely to trigger NREM-related CPNBs rather than paroxysmal events from REM sleep.
Our results seem to suggest that the defective arousal system of extrapyramidal patients tend to be more disreactive in NREM sleep than in REM sleep.

Investigation on the signalling pathways controlling Arc protein expression after cholinergic activation in SH-SY5Y neuroblastoma cells and cultured hippocampal slices

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Objectives. The immediate early gene Arc is necessary for consolidation of hippocampal long-term potentiation (LTP) and formation of hippocampus-dependent long-term memory. We have previously demonstrated that Arc translation during a specific, restricted time window is necessary for maintenance of the late phase of LTP in the rat dentate gyrus. Rapid Eye Movement Sleep (REMS) and its associated increase in cholinergic activity have been proposed to modulate hippocampal synaptic consolidation by promoting plasticity-related gene expression as well as LTP maintenance. Although Arc transcription in response to the muscarinic acetylcholine receptor (mAChR) agonist carbachol has been shown, neither the molecular mechanisms leading to Arc translation, nor the dynamics of Arc protein in the hippocampal network have been clearly described in the context of cholinergic activity. Here we investigated Arc expression after cholinergic activation by carbachol in both SH-SY5Y neuroblastoma cells in culture and organotypic hippocampal slice culture (OTSC).

Methods. OTSC were prepared from postnatal day 5 to 7 rats and biolistically transfected 3 days later with CSIV-SARE-ArcMin-d2EGFP, a plasmid expressing d2EGFP under control of Arc minimal promoter fused to the Synaptic Activity-Responsive Element (SARE). Both OTSC and SH-SY5Y cells were pretreated with various inhibitors or vehicle for 30 minutes and stimulated with 50µM carbachol for 2 hours. SH-SY5Y lysates were processed for western blotting and organotypic slices were finally fixed and observed under fluorescent microscope.

Results. A five-fold increase in Arc protein levels was found in SH-SY5Y cell lysates 2 hours post carbachol application. Carbachol-induced Arc protein expression was completely abolished by the MEK inhibitor U0126 but remained unaffected by the mTOR inhibitor Rapamycin. Carbachol-induced increase in Arc protein levels was not altered by CGP57380, an inhibitor of the kinase MNK1 which links ERK-signalling with translation initiation. Ongoing experiments in transfected OTSC will indicate whether Arc expression is similarly modulated under carbachol treatment.

Conclusion. We are able to show that Arc protein is expressed upon mAChR-stimulation by carbachol in SH-SY5Y cells and that this expression is controlled by ERK-signalling. We also show that carbachol-induced Arc protein expression is independent of both mTOR- and MNK1-signalling.

Cortical gene expression during Paradoxical sleep as revealed by cDNA microarray and qPCR

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Paradoxical sleep (PS), the state during which dreams occurs is present in mammals and birds. Its function remains unknown although several studies indicate that it might play a role in learning and memory. It has been named PS because the EEG shows an activity similar to waking while the muscle tone is completely abolished. To investigate what modifications PS may bring at the molecular level, we profiled gene expression in the hippocampal formation and neocortex in rats with different quantities of PS by cDNA microarrays approach.

The first group of rats (n=12) was deprived of PS by the multiple platform method during 78h, the second group of rats was allow to recover from this deprivation during 6 hours (n=12), the third group of rats remained in their home cage during all the protocol (n=12). All animals were sacrificed at the same time of the day. Total mRNA was extracted from neocortex and hippocampal formation and then hybridized on Affymetrix cDNA microarrays. Quantitative PCRs were then made to validate the results of the microarrays.

The expression of 83 and 73 transcripts was modified by the protocol in the hippocampal formation and neocortex, respectively. Only 18 of these transcripts were common between the 2 structures and their expression level was modified in opposite way for 7 of them. Genes from this group such as c-Fos, Arc and Homer1a have been implicated in synaptic plasticity, learning and memory. They increased their expression level in the neocortex after PS deprivation and on the contrary specifically after PS recovery in the hippocampal formation. Finally, the genes with an expression similarly modified in the both structures increased their expression after PS deprivation and are involved in metabolism regulation.

In conclusion, our molecular results indicate that PS modifies gene expression differentially in the neocortex and the hippocampal formation.

Visuomotor learning and sleep slow-wave activity in children, adolescents and adults

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Objectives. There is increasing evidence that sleep has beneficial effects on learning processes in a variety of tasks [1, 2]. In several studies post-sleep performance improvement (PSLIMP) was related to changes in slow-wave activity (SWA, 1-4.5 Hz) during NREM sleep [3-5]. These changes in SWA were suggested to reflect plastic changes [6]. However, only a small number of studies investigated PSLIMP in children [7, 8], and the results were not related to EEG changes. Here we examined the effects of a rotation learning task on SWA in subjects of different ages.
Methods. Sleep high-density EEG (128 channels) was recorded in 41 healthy subjects (8.7-25.0 y, 29 males) during two separate nights. SWA was calculated for the first four sleep cycles for each night. Before sleep subjects completed either a rotation learning task or a motor control condition. They were retested the following morning. PSLIMP was calculated as the difference between evening and morning performance in subject with at least 50% accurate movements (n=29). To test for age differences, the sample was divided into three age groups (8-12y, 12-18y, 18-25y).
Results. SWA topography was highly reproducible for the two conditions. A contrast between the two conditions revealed significant local increases of SWA over a left frontocentral and a right parietal region after learning (mean ± SE frontocentral: 10.7% ± 2.3, parietal: 10.3% ± 2.1, $p<0.05$). Subjects exhibited a PSLIMP independent of age (mean ± SE: 8-12y, 31% ±9.7; 12-18y, 24.9% ±8.7; 18-25y, 16.8% ±9.2). Furthermore for children and adolescents, PSLIMP was correlated with the parietal SWA increase in the first sleep cycle ($R= 0.4$, $p<0.05$, $n= 22$). The frontocentral increase of SWA showed a relationship to probabilistic sequences learning ($R=0.6$, $p<0.05$, $n=10$).
Conclusion. Even though the typical age-related differences in SWA are substantial, our results show that children and adolescents benefit similarly from sleep in a visuomotor learning task. Confirming earlier work, PSLIMP was correlated with changes of SWA over the region that was responsible for learning the task [3-5]. This observation strengthens the assumption that changes in SWA might be a result of plastic changes. In contrast to earlier studies using the same task, we found an involvement of frontal regions. This might be due to the simplified version we used which led to probabilistic sequence learning.

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The effects of 40 hours of sleep deprivation and recovery night on circadian profile of human immune cells

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Objectives. Sleep is often considered a restorative process with supportive influences on immune system. On the other hand there is a common belief that sleep deprivation has negative consequences on immune system. Studies showed that sleep deprivation has a negative influence on immune system and health. Disruption of the regular sleep-wake cycle through sleep deprivation may influence the immune system. Our interests were to examine the influence of acute 40 hours of sleep deprivation under light conditions and recovery night on circadian profile of peripheral lymphocyte subsets (CD3, CD4, CD8, CD19) and NK cells.

Methods. Blood samples were drawn from nine healthy young volunteers at 4-hour intervals for two consecutive nights, including a night of total sleep deprivation (first night) to determine cell counts of lymphocyte subsets and NK cells. Diurnal variations of cells were tested using analysis of variance (ANOVA). Value of $p < 0,05$ was considered significant. The single cosinor method adapted to a 24-hour period was used for analyzing circadian rhythms of cells. Significant variation was considered if the 95% confidence interval did not include the zero value.

Results. Lymphocyte subsets (CD3, CD4, CD19) and NK cells showed significant circadian variation during the 40 hours of sleep deprivation and recovery night. Cell count peak for CD3, CD4 and CD19 was at night and for NK cells in the morning. In contrast lymphocyte subset CD8 did not show any significant circadian variation during the protocol. Comparison of variables between sleep deprived night and recovery night did not show any significant difference.

Conclusions. Our study revealed no differences in circadian profile of CD3, CD4, CD8, CD19 lymphocyte subsets and NK cells during the 40 hours of sleep deprivation under light conditions and recovery night.

Sensing the future: skin temperature predicts lapses in vigilance

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The preoptic area and anterior hypothalamus (POAH) contain neurons that are essentially involved in both sleep- and thermo-regulation. In this area, and several other brain areas involved in sleep regulation, neuronal activity can be modulated by mild warming and cooling of the skin. Previous studies in humans showed that sleep onset latency and performance on a sustained vigilance task are sensitive to mild skin temperature manipulation[1,2,3]. So far little is known about the predictive properties of unmanipulated skin temperature for lapses in vigilance. We performed a validation of the predictive value of spontaneous fluctuations in skin temperature for the risk of lapses and slow reactions in a sustained vigilance task. Eight healthy participants (5 males, 22-47 years of age) underwent vigilance assessment for two days, in 4 task sessions per day. The four consecutive task sessions started at 09.00 with two hour intervals. During each session, participants were asked to perform a psychomotor vigilance task for 20 minutes while sitting in a dimly lit room. Skin temperature was monitored at several locations throughout the task, whereafter temperature in relation to response speed and lapses were analyzed. Especially proximal skin temperature measured subclavicularly was able to predict lapses in vigilance. These findings are consistent with earlier studies which showed that manipulation of proximal skin temperature is able to influence both sleep onset latency as well as vigilance, thereby strengthening the arguments for the hypothesis that skin temperature is a causal element in the sleep/wake cycle[1].

KEY WORDS: Skin temperature, Vigilance, Attention

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Experience of sleep laboratory from cluj napoca, romania, in treating patients with obstructive sleep apnea syndrome

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Many clinical studies support the association of obstructive sleep apnea syndrome (OSAS) with metabolic syndrome and OSAS is also independently associated with an increased number of cardiovascular risk factors included in metabolic syndrome (MS). The aim of this study was to evidence the presence of MS in patients who accepted to follow the treatment with positive pressure for OSAS, because in our country the treatment for this disease is not supported by health insurance.

Material and methods. From 355 patients investigated and diagnosed with OSAS in our sleep lab from December 2005 to December 2009 only 68 patients could afforded the treatment. We performed poligraphy at these patients and we also evaluated the anthropometric data, as well as the assessment of cardiovascular risk factors, we monitories the presence of HTA, diabetes mellitus and MS conform IDF criteria.

Results. From 68 patients 56 were males, 54 with MS and 12 females all with MS. In males average of: IA/H= 64,62; desaturation index= 56,308; SaO2= 89,21%; nadir SaO2 65,46%; GGT = 60,98 UI/l; blood sugar = 138,66 mg/dl; cholesterol= 216,11 mg/dl; HDL- cholesterol = 52,11 mg/dl; triglycerides =260,407 mg/dl, abdominal circumference =126 cm. From males patients 33 had HTA and 14 diabetus mellitus. In females average of: IA/H= 64,21; desaturation index= 61,87; SaO2= 88,58%; nadir SaO2 = 61,83%; GGT = 41,225 UI/l; blood sugar = 127,5 mg/dl; cholesterol= 203,83 mg/dl; HDL-cholesterol= 37,1 mg/dl; triglycerides=174,2 mg/dl ,abdominal circumference =130,9 cm. From females patients 10 had HTA and 4 diabetes mellitus.

Conclusions. The cardiovascular risk among small proportion of patients who followed the treatment is very high.

Sleep changes under condition of modeling of longtime space mission

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Objectives. Chronical and acute stress have an influence on the sleep and usual disrupt it. But mechanisms of development of sleep disorders are unclear. This experiment was performed to study sleep and wakefulness changes during 105-days stress of isolation in the model of the spaceship (project Mars-105).

Methods. 6 healthy men from 25 to 40 years old (in average 33.0±5.7) were studied by questionnaires (sleep dairy) and polysomnography (PSG). The age of examiners was from 25 to 40 years (in average 33.0±5.7). The examiners filled sleep dairy once in 6 days. PSG-recording included electromyography, electrooculography and electroencephalography (6 channels) registration and scored manually. PSG recorded once 2 weeks before, 2 times during (9-14 and 83-88 day of isolation) and once 2 weeks after isolation. Each registration included 2 nights.

Results. Sleep dairy: during isolation all participants have changes in sleep-wake cycle. They go to sleep at irregular time and usually late at night (in average at 1:15 a.m.). Sometimes they have problems to fall asleep (in average sleep latency was 16 minutes), night awakenings (in average once a night), sleepiness (in 58% of all days) and daytime sleep (2-3 times every 5 days).
PSG: in 17.2% of all findings examiners have sleep latency more than 20 minutes, in 20.7% wakefulness inside the sleep more 30 minutes and in 3.4% long both falling asleep and awakenings. Most of nights with any “pathology” were recording on 83-88 day of isolation. Amount of sleep disturbance increase in comparison with background recordings ($p<0.05$, Fisher’s method) and recording during 9-14 day of isolation ($p<0.05$). Sleep structure have changed 2 weeks before start of the isolation (probable, intensive timetable is the reason of it). Percentage of delta-sleep and REM-sleep decrease in comparison with the index for healthy the same age people before experiment. During the experiment the amount of deep sleep and REM don’t change significantly, but sleep latency increase. After the isolation delta-sleep duration increase and sleep latency decrease, but REM-sleep amount stay low.

Conclusion. Under the influence of chronical stress of isolation sleep changes are similar to sleep of patient with some sleep disorders. They include signs of delayed circadian rhythmus, insomnia with problems to fall asleep, night awakenings and daytime sleep.

Cardiovascular risk in patients with moderate and severe obstructive sleep apnea syndrome

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Obstructive sleep apnea syndrome (OSAS) is a condition involved in the development of new cardiovascular disturbances or in aggravating the old one, and for that it is imperative to be treated early and accurate.
Aim: to evaluate cardiovascular risk in moderate and severe OSAS patients by SCORE and also to observe how each item of this quantification system is involved in increasing the risk of developing a fatal cardiovascular event in the next ten years.

Methods. We evaluated 95 patients with moderate or severe OSAS, polysomnographically recorded between January 2007-January 2009 in our sleep lab and we corroborate the data from this recordings (apnea-hypopnea index-AHI, time bellow 80% oxygen saturation – TS80) with anthropometric data, blood pressure values, smoking habits, and blood test analysis.

Results. There is a strong correlation between cardiovascular risk evaluated by SCORE and the severity of OSAS (r=0.628, P=0.001) and also between arterial hypertension (AH) and TS 80. Prolonged intermittent hypoxia is also associated with cholesterol level.

Conclusion. The severity of OSAS is strongly positive correlated with cardiovascular risk and AH, even after adjusting for body mass index and for sex. Smoking does not aggravate OSAS but increases the cardiovascular risk. These results count for the need of rapid diagnostic and early treatment of OSAS.

The characteristics of sleep during early period of pregnancy in rats

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Objectives. A number of studies have been carried out to describe sleep structure in pregnant women and animals. Nevertheless methodical limitations and differences do not make it possible to draw an integrated picture of sleep features during this period and especially its early stage. In the present study we performed a detailed investigation of sleep pattern in rats during the first week of pregnancy.

Methods. EEG, hippocampal theta-activity and locomotor activity were recorded twenty-four-hours in 18 female Wistar rats. The control (non-pregnant rats) and the experimental groups included 12 and 6 rats respectively. The recordings were performed during 3 consecutive days in non-pregnant rats and during 1-7th days of pregnancy in animals of the experimental group in standard conditions. We evaluated the percentage of NREM and REM sleep for 24 h, 12 h light and dark periods and hourly intervals over the day, the number of brief awakenings, the number of episodes of wakefulness, NREM and REM sleep. In addition we analyzed the distribution of NREM and REM sleep episodes according to their duration. Measures for each day of pregnancy were compared with averaged measures for three days of recordings in non-pregnant control rats.

Results. REM sleep quantity was increased in the dark period on the second day of pregnancy. NREM sleep percentage did not differ from the control level for any of the studied time periods. At the same time NREM sleep was more fragmented and less intensive during the first week of pregnancy. We also found that daily sleep pattern was modified in pregnant rats. The distribution of NREM and REM sleep episodes durations in 12 h light and dark periods changed significantly with the start of pregnancy. As a result disappearance of day-night difference for this sleep parameter on days 2-5 of pregnancy was clearly seen.

Conclusion. *In rats during the first week of pregnancy sleep structure changes* significantly while the amount of both NREM and REM sleep remain the same as in non-pregnant animals. The mechanisms for these changes should be further investigated.

Sleep and metabolism: sleep regulation in a USF1 knockout mouse model

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Objectives. There is increasing evidence of a link between metabolic disorders and sleep problems. Upstream transcription regulator (USF1) gene plays a key role in regulating genes that control lipid and glucose metabolism. Genetic variation in the USF1 gene predisposes to hyperlipidemia and elevated levels of blood triglycerides; known risk factors for metabolic syndrome and type 2 diabetes. USF1 influences metabolism in USF1 over-expressing mouse model (Wu et al., Upstream transcription factor 1 influences plasma lipid and metabolic traits in mice. Human molecular genetics. 2010). Our aim was to investigate the effects of USF1 gene on sleep and circadian rhythm.

Methods. We used USF1 knockout mice (wild type, WT; heterozygous, HT; knock out, KO) with decreased lipid and glucose levels for this study. We measured the electroencephalogram (EEG) and daily activity of the mice during baseline and 6h sleep deprivation.

Results. In baseline conditions the HT/KO mice were less active (mean distance moved) and spent more time in non-rapid eye movement (NREM) sleep during dark period compared to the WT mice ($p<0.05$), whereas during light period the HT/KO mice spent less time in NREM sleep. During a 6h sleep deprivation the HT/KO mice needed twice as many interventions as the WT mice ($p<0.05$) to stay awake and the NREM recovery sleep following sleep deprivation was attenuated.

Conclusion. Preliminary analysis revealed that USF1 knockout mice have problems in sleep regulation, most probably due to the lower levels of blood energy metabolites. Our finding further supports the notion that lipid levels directly affect sleep and circadian rhythm.

Effect of weight loss on inflammatory markers in overweight patients with mild obstructive sleep apnoea

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Objectives. Obstructive sleep apnoea (OSA) has been proposed to be an important risk factor for mortality, particularly due to coronary artery disease. Low-grade inflammation may be one mediating mechanism for increased risk of cardiovascular diseases in OSA. Even a mild OSA has been found to be associated with the activation of the pro-inflammatory systems. However, little is known about the effect of intervention on inflammation in early stages of OSA. There is some evidence that mild OSA may increase the levels of both pro- and anti-inflammatory mediators similar to early stages of type 2 diabetes mellitus. The aim of this randomised, controlled study was to determine the impact of lifestyle changes aimed at weight reduction on inflammatory markers in overweight patients with mild OSA.

Methods. Overweight (body mass index 28-40 kg/m^2) adult patients with mild OSA (apnoea-hypopnoea index 5-15/hour) were randomised to lifestyle intervention group or control group. The intervention group completed 1-year supervised lifestyle intervention with weight reduction. The control group received routine lifestyle advices. Circulating concentrations of pro-inflammatory [high sensitivity C-reactive protein(hs-CRP), interleukin (IL)-1-beta, IL-6 and tumour necrosis factor –alpha (TNF-alpha)] and anti-inflammatory [IL-1 receptor antagonist (RA) and IL-10] mediators were measured before and after the 1-year intervention.

Results. 59 patients completed the 1-year follow-up, (N=28 in the intervention group and N=31 in the control group). There was significant reduction in weight favouring the intervention group [-10.7 kg vs. -2.9 kg, (P<0.001)]. Total AHI also decreased significantly in the intervention group, but the difference between the groups was not statistically significant. The concentrations of pro-inflammatory mediators, hsCRP and IL-6, decreased significantly in both groups. Although the changes in inflammatory biomarkers favoured the supervised lifestyle intervention, the only significant reduction observed between the study groups was for the anti-inflammatory IL-1RA. The changes in body composition were found to be the most attributable factors for the reduction. In multiple regression analysis, improving nocturnal respiratory function partly explained the changes in hsCRP and TNF-alpha. The decrease in IL-1RA was best explained by improving insulin resistance. Additionally, improving total body composition variables (mainly BMI) had several borderline significant associations with hsCRP and IL-6 but, these were dumped by stronger predictors.

Conclusion. Weight loss resulted in reductions in concentrations of both pro- and anti-inflammatory mediators in overweight patients with mild OSA, overall favouring the supervised intervention. Furthermore, our results suggest that in overweight patients with mild OSA, changes in immune mediators could be related not only to changes in body composition but also to improved sleep disordered breathing and insulin resistance.

Sleep disturbances as a predictor of cause-specific work disability and delayed return to work

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Objectives. In the working population, about 30-50% experience sleep disturbances occasionally and up to 10% meet the criteria for clinical insomnia diagnosis. Recent studies have found that sleep disturbances predict subsequent occupational disability, but underlying causes and associations with subsequent return to work are not known. We aimed to examine sleep disturbances as a predictor of cause-specific work disability and delayed return to work.

Methods. This prospective observational cohort study included 56,732 local government employees (mean age 44.4, 80% female) in 10 towns and 21 public hospitals in Finland (the Finnish Public Sector Study). The participants were at work and free of work disability at the study inception. Survey data on sleep disturbances were linked with records of work disability (≥90 days sickness absence, disability pension, or death) obtained from national registers.

Results. During a mean follow-up of 3.3 years, incident diagnosis-specific work disability was observed in 4,028 (7%) employees. Of those, 2,347 (60%) returned to work. Sleep disturbances during 5-7 nights per week predicted work disability due to mental disorders [hazard ratio (HR) 1.6, 95% confidence interval (CI) 1.3-1.9] and diseases of the circulatory system (HR=1.6, 95% CI 1.2-2.1), musculoskeletal system (HR=1.6, 95% CI 1.4-1.8) and nervous system (HR=1.5, 95% CI 1.0-2.2), and injuries and poisonings (HR=1.6, 95% CI 1.2-2.1) after controlling for baseline age, sex, socioeconomic status, night/shift work, health behaviours (e.g., smoking, exercise), diagnosed somatic diseases, use of pain killers, depression, and anxiety. In addition, sleep disturbances prior to disability were associated with higher likelihood of not returning to work after work disability from musculoskeletal diseases (HR=1.2, 95% CI 1.1-1.7) and, in men, after work disability due to mental disorders (HR=4.4, 95% CI 1.7-11.1).

Conclusions. Sleep disturbances are associated with increased risk for subsequent disabling mental disorders and various physical illnesses. They also predict the outcome of work disability due to musculoskeletal disorders.

Effect of sleep deprivation on neurochemical status in the rat basal forebrain in clomipramine model of depression

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Depression is often associated with sleep problems which may occur due to disruptions in sleep homeostasis. The normal homeostatic sleep response consists of increased slow wave activity after prolonged waking, as well as increased extracellular concentrations of adenosine and nitric oxide (NO) in the basal forebrain (BF) during the waking period. We investigated the effect of sleep deprivation (SD) on the levels of adenosine, NO and brain-derived neurotrophic factor (BDNF) in the BF in an animal model of depression.

Male rat pups treated with clomipramine (20 mg/kg, s.c.) twice daily from postnatal day 5 to 21 were subjected to 3 hours SD at the age of 3 months. Using in vivo microdialysis, samples for adenosine and NO measurement were collected before, during and after SD. Adenosine was measured using high-performance liquid chromatography and NO was assessed using a nitrate/nitrite fluorometric assay kit. For assessment of BDNF and iNOS protein levels, the brain tissues were collected immediately after the SD and measured by ELISA kit and immunoblotting.

Clomipramine-treated rats (CLI-rats) were characterized by low basal level of adenosine (45.3±2.2%; p<0,001) and BDNF (72.9±11.4%; p=0.2) and by high basal level of NO (172.2±23.3%; p=0.003) and iNOS (137.0±16.8; p=0.1). The low basal levels of BDNF and adenosine may indicate deficiencies in neural plasticity while elevated NO level may indicate the activation of the immune system – findings that may be associated with depression.
During SD the levels of adenosine and NO increased gradually in the extracellular space of BF in control rats, inducing increase in slow wave activity. Despite the low basal level of adenosine of CLI-rats the homeostatic response after 3 h SD was intact (143.2±15.7% as compared with own baseline; p=0.002). However, the level of NO had a decreasing trend during SD (69.0±9.7%; p=0.07). SD reduced also BDNF level of both CLI-rats (69.6±8.3%; p=0.12) and control rats (57.0±9.7%; p=0.04).

The decreased homeostatic response (less NO, but not adenosine) after SD in CLI-rats rats unlike in controls, as well as lower levels of BDNF allow us to suggest that depression can deteriorate sleep by disturbing the mechanism of sleep homeostasis. Taken together these data provide insight to understanding of the mechanisms of interaction between sleep and depression.

Sleep-dependent consolidation of temporal order in episodic memories

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Meanwhile there is plenty of evidence indicating that sleep has a beneficial effect on declarative and procedural memory consolidation. Here we study the influence of sleep versus sleep deprivation on temporal order in episodic memories. 34 young participants either slept or had to stay awake during the whole night after learning various stories. Each story consisted of 12 pictures (6 faces and 6 objects) presented in sequence and participants had to invent a story with themselves being a part of it. In addition to a previous screening/adaptation night the “sleep group” slept in the sleep laboratory after learning with full polysomnography attached. Retest was done the next morning, as well as after 2 recovery nights in order to circumvent fatigue effects of the sleep-deprived group.

Results revealed that performance in temporal order memory was only deteriorated in the post-training sleep deprived group. Recognition of neutral images was faster than that of negatively rated items. Furthermore, we report a positive relationship of rapid eye-movement (REM) sleep after learning and performance in temporal order recall. Last but not least we could confirm earlier findings reporting positive association of (fast) non-REM sleep spindles and cognitive abilities (as revealed by the Wechsler Memory Scale- revised and Raven`s Advanced Progressive Matrices).

This repeatedly found general association might indicate that sleep spindles are a good indicator for cognitive capability simply because they allow a rough estimation of the effectiveness of thalamocortical connectivity.

Sleep deprivation fails vanishing pseudoneglect

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Objectives. A slight but consistent right visual field pseudoneglect [i.e. a leftward (LW) attentional bias] is observed within the healthy population. Right hemispheric (RH) dominance in alertness regulation is usually supposed to explain this phenomenon. It has been shown using a landmark (LDM) task that sleep deprivation (SD) induces a rightward shift in attention abolishing this LW bias (Manly et al. 2005 Neuropsychologia), suggesting that SD preferentially affect the RH. However, total amount of SD, moment of testing and fatigue were not controlled across participants in this study conducted with shift-workers. Here we aimed at replicating this effect in a controlled setting.

Methods. Thirteen healthy right-handed volunteers (6 males; mean age= 23.2 years, sd= 1.8) participated in an 11 days follow-up study. The LDM task was administered 6 times: at 9:00 p.m. on Day 1, 4, 8 and 11, and at 7:00 a.m. on Day 2 and 9. Half of participants were sleep deprived between Day1 and 2, the other half between Day 8 and 9, under controlled conditions.
Each session consisted of 100 lines evenly bisected and 100 lines with the vertical divider shifted 5mm on the left or on the right. Lines were presented in random order on a computer screen for 1000ms. A mask was presented after each line and participants had to judge which section of the line was either the longest or the shortest according to the displayed instruction. Participants responded with right index and middle finger. In each session, the LW bias was calculated as the proportion of left longest/right shortest responses for the evenly bisected lines.

Results. Participants judged even bisected lines as “left longer/right shorter” in 73.9% (sd=18.4) of the cases at Day 1 (P<.001 for t-test against 0), 73.5% (sd=19.7; P<.001) at Day2, and 71.7% (sd=24.1; P<01) at Day4 during the regular sleep week, and in 75.3% (sd=15.2) of the cases at Day1 (P<.001), 66.3% (sd=21.3; P<.001) at Day2, and 77.1% (sd=14.1; P<01) at Day4 during the SD week. A repeated ANOVA with Condition (sleep vs. deprivation) and Session (Day1 vs. Day2 vs. Day4) factors conducted on arcsine transformed proportional data failed to significant effects (all Ps>.11).

Conclusion. As expected, our participants exhibited a strong LW bias all along the sessions. However, a total night of SD failed to reduce this bias. We hypothesize that circadian confounds or fatigue effects after shift work, more than SD *per se,* may explain previous modulation of the LW bias.

Linking Sleep, Behaviour and Cognition in Childhood – a Meta-Analysis

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Objectives. Past research has shown that sufficient adult sleep is vital for daytime functioning, with sleep deprivation resulting in disrupted daytime performance. Less is known about the consequences of sleep loss in childhood. The recent years have seen an increased interest in childhood sleep and its relationship to daytime functioning, however results appear inconclusive. It therefore seems timely to aggregate all previous findings by meta-analysis to determine the status of, and gaps in, our current knowledge.

Methods. An extensive literature search was performed to find all research incorporating an objective measure of sleep, a measure of daytime functioning and a healthy childhood participant group. All relevant articles were objectively scored by two reviewers, and methodological and statistical aspects were imported into Comprehensive Meta-Analysis software. Independent effect sizes were calculated and split into 3 dimensions: Cognition, Behaviour, or Sleepiness. Separate meta-analyses, using random effect models, tested for the strength of a possible correlation between sleep duration and each of the three dimensions of daytime functioning.

Results. Eighty relevant studies were found. The meta-analyses revealed significant relationships between sleep and each of the 3 dimensions of daytime functioning. Sleep duration and cognitive performance were positively correlated, $r = 0.090$ ($p < 0.001$). Sleep duration and behavioural problems were negatively correlated, $r = -0.075$ ($p < 0.001$). Finally, sleep duration and daytime sleepiness showed a significant negative correlation, $r = -0.093$ ($p < 0.001$).

Conclusion. This meta-analysis on sleep and daytime functioning in childhood conclusively reveals significant correlations between sleep, cognition and behaviour. Although the overall effect sizes are small, they confirm the existence of a previously disputed relationship. In light of the current results we would recommend ensuring that children obtain an adequate night's sleep duration.

PERIOD3 polymorphism, subjective and physiological sleepiness during day and night driving on real roads

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Objectives. Sleep loss and time of day strongly affect sleepiness at the wheel. However, large individual differences exist. A potential underlying mechanism of these variations in vulnerability is a variable number (4 or 5 repeats) tandem repeat polymorphism in the clock gene PERIOD3 (PER3). The objective of the present study was to examine the effect of the PER3 genotype and prolonged wakefulness on driving performance, subjective and physiological sleepiness during actual driving on a real road.

Methods. 21 healthy subjects, 11 homozygous for the $PER3^{4}$ allele, 10 homozygous for the $PER3^{5}$ allele (mean age=45 years, 50% females), drove during the day, evening and night for approximately 90 minutes. Subjective sleepiness was assessed every 5 minutes using the Karolinska Sleepiness Scale (KSS). Physiological sleepiness was continuously measured using EEG recording (Fz - A1, Cz - A2, Oz -Pz). For analyzing the EEG, we used higher EEG frequencies (96 – 124hz) as ratios using log transformed theta, alpha, sigma and beta power spectrum bands. Statistical analysis was carried out by a mixed linear regression with fixed effects for condition, time (continuous), gene, time^2, random intercept and random effects for condition and time.

Results. KSS showed significant main effects for condition, time (both $p < .001$), time^2 ($p = .046$), as well as significant interactions of condition*time ($p < .001$) and condition*time*gene ($p = .001$), indicating increased sleepiness during the night drive and particularly so in the $PER3^{5/5}$ group. Preliminary EEG-results show, in the theta-range, only the condition ($p < .001$) was significant (increased theta during the night). In the alpha-range, condition, time, time^2 and the interaction condition*time were significant (all $p < .001$), indicating increased alpha activity during the night. In the sigma-beta spectrum, time ($p = .047$), condition, condition*time (both $p < .001$) and the 3-way interaction condition*time*gene was significant ($p =.003$), indicating a nighttime decrease in the 12-32hz spectrum in subjects with the $PER3^{5/5}$ genotype.

Conclusion. Both KSS and EEG were affected by driving duration and increasing time awake. Furthermore, the results indicate that $PER3^{5/5}$ individuals have higher values of subjective and physiological sleepiness during night driving on a real road.

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Role of the lateral paragigantocellular nucleus in the regulation of paradoxical sleep in the rat

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The genesis of paradoxical sleep (PS) requires the activation and inactivation of several populations of neurons organized in networks in the brainstem. The lateral paragigantocellular nucleus (LPGi) might be an important inhibitory afferent of the locus coeruleus and dorsal raphe nuclei neurons that are silent during PS. Indeed, during the PS hypersomnia following a specific deprivation, the LPGi contains numerous GABAergic/Fos labeled neurons, suggesting that the LPGi could contain neurons active during PS (PS-On neurons). We aimed at characterizing the pattern of activity of the LPGi neurons in relation to the sleep-waking cycle and to identify their afferent and efferent projections. Unit extracellular recordings were obtained in the unanesthetized head-restrained rat preparation. CTb (retrograde tracer) and PHA-L (anterograde tracer) were ejected in the LPGi in the same animals and a PS hypersomnia was obtained after PS deprivation. Immunohistochemistry of CTb/Fos and PHAL/Fos was performed.

The results show that the LPGi contains neurons firing specifically during PS (PS-ON) with some of them starting before the onset of PS. The LPGi also contains neurons inactive during PS (PS-OFF neurons). The anatomical results show that the LPGi is reciprocally connected with autonomic areas as well as the brainstem areas involved in the genesis of PS : the sublaterodorsal nucleus in the pons, the ventrolateral periaqueductal gray and the dorsal reticular formation in the mesencephalon.

The observation of CTb/Fos neurons in these areas, during the PS hypersomnia, suggests that they control the activity of the LPGi neurons during PS. Afferent connections also arise in the dorsal hypothalamus and the zona incerta. In the latter area, some retrogradelly labelled neurons express MCH, neuropeptide likely involved in the homeostatic control of PS. Our results argue for a significant role of the LPGi in network of PS regulation.

Sleeping habits and sleep disorders prevalence in infants aged 6 and 15 months

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Objectives. Describing sleeping habits and prevalence of sleep disorders in population aged 6 and 15 months, determining associated risk factors and improving knowledge about sleep features and disorders in this group of population in the city of Cuenca (Spain).

Methods. Observational descriptive cross-sectional study in infants aged 6 and 15 months attending arranged appointments at Pediatrics office in Cuenca city during 3 months (n=214).
Measures: Brief screening Questionnaire for Infant Sleep Problems (BISQ) answered by parents, as well as a questionnaire about socio-demographic data.

Results. In socio-demographic data we find higher prevalence of sleep disorders among females and immigrants. It's also related with lower mother's academic degree. About sleeping habits we find higher prevalence of individual cradle in parents' room, supine position and night sleep time ≤9h in infants aged 6 months; whereas sleeping in parents' bed, going to bed at 22h or later and starting sleep alone were more prevalent in infants aged 15 months. Bad sleeping habits showed relation to higher prevalence of sleep disorders.
Overall prevalence of sleep disorders is 7.9% (10.1% in infants aged 6 months, 4.7% in aged 15 months). Severe sleep disorder is observed in 2.3% of 6 month-aged infants and in 2.4% of 15 month-aged infants. Symptoms related to insomnia (late sleep onset, few night sleep hours, nocturnal awakenings) were present in 92.3% of infants aged 6 months and in 100% aged 15 months. Besides, poor quality of sleep, slight sleep disorder, late sleep onset and nocturnal arousals were more prevalent in infants aged 6 months than in aged 15 months.

Conclusion. Changes in sleep features in infants aged 15 months respecting those aged 6: reduction in nightime and rise in daytime sleep, trend to sleep in room apart from parents and less need to sleep-induction mechanisms. Prevalence of sleep disorders in infants aged 6 and 15 months is low. The most common symptoms are those related to insomnia. These disorders are related with socio-demographic data. We demonstrate that they also depend on sleep habits, therefore they are easy to prevent by educating parents in them.

Investigation on the signalling pathways controlling Arc protein expression after cholinergic activation in SH-SY5Y neuroblastoma cells and cultured hippocampal slices

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Objectives. The immediate early gene Arc is necessary for consolidation of hippocampal long-term potentiation (LTP) and formation of hippocampus-dependent long-term memory. We have previously demonstrated that Arc translation during a specific, restricted time window is necessary for maintenance of the late phase of LTP in the rat dentate gyrus. Rapid Eye Movement Sleep (REMS) and its associated increase in cholinergic activity have been proposed to modulate hippocampal synaptic consolidation by promoting plasticity-related gene expression as well as LTP maintenance. Although Arc transcription in response to the muscarinic acetylcholine receptor (mAChR) agonist carbachol has been shown, neither the molecular mechanisms leading to Arc translation, nor the dynamics of Arc protein in the hippocampal network have been clearly described in the context of cholinergic activity. Here we investigated Arc expression after cholinergic activation by carbachol in both SH-SY5Y neuroblastoma cells in culture and organotypic hippocampal slice culture (OTSC).

Methods. OTSC were prepared from postnatal day 5 to 7 rats and biolistically transfected 3 days later with CSIV-SARE-ArcMin-d2EGFP, a plasmid expressing d2EGFP under control of Arc minimal promoter fused to the Synaptic Activity-Responsive Element (SARE). Both OTSC and SH-SY5Y cells were pretreated with various inhibitors or vehicle for 30 minutes and stimulated with 50µM carbachol for 2 hours. SH-SY5Y lysates were processed for western blotting and organotypic slices were finally fixed and observed under fluorescent microscope.

Results. A five-fold increase in Arc protein levels was found in SH-SY5Y cell lysates 2 hours post carbachol application. Carbachol-induced Arc protein expression was completely abolished by the MEK inhibitor U0126 but remained unaffected by the mTOR inhibitor Rapamycin. Carbachol-induced increase in Arc protein levels was not altered by CGP57380, an inhibitor of the kinase MNK1 which links ERK-signalling with translation initiation. Ongoing experiments in transfected OTSC will indicate whether Arc expression is similarly modulated under carbachol treatment.

Conclusion. We are able to show that Arc protein is expressed upon mAChR-stimulation by carbachol in SH-SY5Y cells and that this expression is controlled by ERK-signalling. We also show that carbachol-induced Arc protein expression is independent of both mTOR- and MNK1-signalling.

Heart rate and heart rate variability in primary insomnia

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Objectives. According to epidemiological studies, insomnia is associated with cardiovascular mortality. However, it is yet to be determined whether this link is mediated by known cardiovascular risk factors. The current study aimed at investigating the association between primary insomnia, defined as sleep disturbance in the absence of any other pathology or substance intake, and alterations in polysomnographically determined nocturnal heart rate and heart rate variability.

Methods. A total of 4581 nocturnal short-term electrocardiographic recordings (5 minutes each) from 104 participants (58 with primary insomnia, 46 healthy controls) were evaluated for heart rate as well as for time and frequency domain measures of heart rate variability.

Results. In the primary insomnia group, we found a reduced day-to-night HR difference and a reduced SDNN compared to healthy controls. However, between-group differences in resting HR were not found and previous results of an increase in sympathovagal balance and a decrease in parasympathetic nocturnal activity could not be found in our sample.

Conclusion. A reduced day-to-night heart rate dipping and a reduced overall heart rate variability might be the link between insomnia and cardiovascular morbidity and mortality.

Performance of different evaluation scales of neurocognitive function in Sleep Apea Syndrome

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Objective. Sleep apnea syndrome (SAS) has multisystemic manifestations including neurological and cognitive.Neurocognitive impairment in SAS is manifested both in terms of altering cognition and alertness, up to affecting the quality of life and increasing the risk of workplace accidents / traffic accidents.The aim of this study is to determine the capacity of specific tests used in our clinic to detect early deterioration of cognitive function and alertness, in patients with severe SAS but without or with minimal sleepiness according to Epworth Sleepiness Scale (ESS).

Methods. A controlled study on 2 groups: first group formed by 56 patients suffering from severe SAS with a low score on ESS compared with the control group formed by 39 individuals without SAS. All subjects had to complete the Epworth Sleepiness Scale (ESS), somnographic or polisomnographic recordings and then a battery of tests aimed to measure the memory impairment, cognitive inhibition, decision making ability, reaction speed and concentrated attention.

Results. In group with SAS, ESS = 9,64 and in control group ESS = 4,73. On a scale of 1-5 at the neurocognitive tests the following scores were obtained: patients with SAS obtained at decision capacity an average score of 3,240 compared to 3,389 obtained by the control group (p = 0,6827), for the short-term memory the SAS group obtained 2,400 and the control group obtained 2,63 (p = 0,503), for focused attention in the SAS group an average score of 2,083 and 2,842 in the control group (p = 0,0476), simple reaction time in the SAS group has a score of 2,909 and 3,222 in control group (p = 0,3466), time of reaction in choosing in the SAS group was 2,800 and 3,056 in the control group (p = 0,3466), and the reaction time in memory accessing in the group with SAS was 2,920 and 3,167 in the control group (p = 0,5194).

Conclusions. 1.In cases of patients with severe SAS without of with low score on ESS there is an absence of early changes in cognition/alertness(short time memory,reaction speed).
2.There is noticed a decreased concentration ability in patients with severe SAS even thou they have low score in ESS.

Contrasting gray and white matter changes in preclinical Huntington disease: An MRI study

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Background. In Huntington disease (HD), substantial striatal atrophy precedes clinical motor symptoms. Accordingly, neuroprotection should prevent major cell loss before such symptoms arise. To evaluate neuroprotection, biomarkers such as MRI measures are needed. This requires first establishing the best imaging approach.

Methods. Using a cross-sectional design, we acquired T1-weighted and diffusion-weighted scans in 39 preclinical (pre-HD) individuals and 25 age-matched controls. T1-weighted scans were analyzed with gross whole-brain segmentation and voxel-based morphometry. Analysis of diffusion-weighted scans used skeleton-based tractography. For all imaging measures, we compared pre-HD and control groups and within the pre-HD group we examined correlations with estimated years to clinical onset.

Results. Pre-HD individuals had lower gross gray matter (GM) and white matter (WM) volume. Voxel-wise analysis demonstrated local GM volume loss, most notably in regions consistent with basal ganglia thalamocortical pathways. By contrast, pre-HD individuals showed widespread reductions in WM integrity, probably due to a loss of axonal barriers. Both GM and WM imaging measures correlated with estimated years to onset.

Conclusions. Using automated, observer-independent methods, we found that GM loss in pre-HD was regionally specific, while WM deterioration was much more general and probably the result of demyelination rather then axonal degeneration. These findings provide important information about the nature, relative staging, and topographic specificity of brain changes in pre-HD and suggest that combining GM and WM imaging may be the best biomarker approach.

Influence of daytime light on nighttime parameters like sleep, melatonin secretion and alertness

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Objectives. Light exposure is known to have long-term therapeutic effects in chronobiologically related disorders like seasonal affective disorder (Lewy et al., 1998), shift work syndrome and even nighttime confusion in Alzheimer disease. However, the influence of daytime light exposure in the healthy population living in a natural environment is widely unknown.
The aim of the current study was to investigate the effects of light exposure during habitual daytime activities on evening alertness and light induced melatonin suppression as well as nighttime sleep in 11 healthy participants (no extreme chronotypes).
Methods. Participants were instructed to maintain their habitual sleep/wake behaviour, controlled by actigraphy. They were instructed to wear *Luxblick* spectacles recording illumination and blue light (lux) on five consecutive days. Each evening participants came to the laboratory, staying in dim light conditions for three hours starting at 7 pm. At 10 pm participants were exposed to light of different intensities and spectra until 10:30 pm and went to bed at 11 pm. Each night sleep was polysomnographically recorded in the lab. Saliva samples to determine melatonin secretion were collected every 30 minutes (every 10 minutes during light exposure) until bedtime. Subjective alertness was determined every 30 minutes until bedtime using a visual analogue scale (Bond & Lader, 1974).

Results. The illumination levels participants were exposed to from 8 to 11 am was significantly associated with melatonin suppression by bright polychromatic blue light in the evening ($r = 0,598$; $p = 0,003$), with Sleep Period Time ($r = 0,329$; $p = 0,05$) as well as Time in Bed ($r = 0,412$; $p = 0,012$). There was a trend towards significance in the correlation between light in the morning and the total amount of REM sleep ($r = 0,28$; $p = 0,096$).

Conclusions. Data show that the amount of morning light is related to subsequent nighttime sleep. Future studies have to show whether daytime light may have an effect on disorders like e.g. primary insomnia as well.

Keywords. polychromatic light, light history, melatonin, polysomnography

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The amount of deep sleep is inversely related to daytime systolic blood pressure in patients with chronic kidney disease

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Objectives. Objective characteristics like the amount of deep sleep (DS) are related to nocturnal blood pressure and dipping. The aim of the present study was to investigate if macrostructural characteristics of sleep can be associated with daytime blood pressure (BP) in patients with chronic kidney disease.

Methods. In the SLeep disorders Evaluation in Patients after kidney Transplantation [SLEPT] Study 100 randomly selected kidney transplanted and 50 dialysed patients on transplantation waiting list were enrolled. Age, gender, details of medical history, information on comorbidity were collected at enrollment. Laboratory data were extracted from medical records. The average of three BP measurements taken during morning hours was calculated. Each patient underwent standard one-night polysomnography.

Results. The mean age was 51+/-13 years and 56% were males. The average of systolic and diastolic daytime BP were 135+/-21 mmHg and 81+/-13 mmHg, respectively. The median (interquartile range) of DS and sleep efficiency was 12(11)% and 80(16)%, respectively. Deep sleep was negatively correlated with daytime systolic BP ($r=-0.31$, $p<0,001$) and also showed a nearly significant weak negative correlation with diastolic BP ($r=-0.16$, $p=0.053$). Sleep efficiency also tended to correlate with systolic BP ($r=-0.15$, $p=0.069$). In a multivariate regression model the amount of DS showed an independent, significant relationship with daytime systolic BP ($B=-0.56$, $p=0.005$) after controlling for age, gender, several relevant clinical factors and sleep-related variables. DS was close to be significantly associated with diastolic BP in a similar model ($B=-0.23$, $p=0.081$). None of the other sleep characteristics, including apnoe-hypopnoe index, showed any significant relationship with daytime BP.

Conclusion. The amount of deep sleep is inversely related to daytime systolic BP in patients with CKD, regardless of many potential confounder variables.

Approaching CPAP adherence through a visual analog scale

* CPAP- continuous positive airway pressure

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Background. Adherence to long-term therapies has been considered the corner stone to assure adequate treatment outcomes for patients with chronic conditions. Our aim is to improve understanding of CPAP users, identifying each patient perception of how easy or difficult is the use of the equipment.

Study objectives.

a) To test a structured visual analog scale (VAS) - where *0: very easier and 10: very difficult* - to assess probability of CPAP adherence;

b) Identify specific problems and motivations related to long-term CPAP use.

Design and methods. Longitudinal prospective study, with 3 observations: initial assessment; first CPAP follow-up (1 month); long-term follow-up (20 months). The studied variables were related to the patient; the OSA stage and severity; treatment characteristics and adverse events; life and biomedical factors; co-morbidities relevantly related to OSA. Statistical data analysis was performed, using SPSS 17.

Results. The study started with 26 men and 8 women, with a mean age 55,2 $\pm$ 13,5, body mass index 34,2 $\pm$ 12,8 Kg/m^2, apnea/hypopnea index 33,8 $\pm$ 20,4 events/hour and an Epworh scale 9,8 $\pm$ 5,9. The mean value obtained at the beginning for the VAS was 3,4 $\pm$ 2,4. The main initial motivational aspects related with CPAP treatment were: sleep quality (14 patients); daily quality of life (13 patients); to minimize OSA symptoms (10 patients). Initial predictable difficulties referred were: mask adaptation (12 patients). Nine patients declared no difficulties.

In the 1st follow-up (1 month) 5 patients quit the studied. Long-term follow-up (18 months) was only performed in 20 patients. The results are shown in the Table

Study aspects	*1st follow-up (1 month)*	*Long-term follow-up (18 months)*
Mean hours of CPAP use hour(h)/day(d)	3,3 $\pm$ 2,4 h/d	3,7 $\pm$ 2,4 h/d
Adherence to CPAP therapy$\geq$ 4,5h/d	41,4%	40%
Epworh scale	7,6 $\pm$ 5,2	6,9 $\pm$ 5,0
VAS	4,9 $\pm$ 3,1	3,7 $\pm$ 2,4
Positive aspects related with OSA treatment:	Sleep quality (9 patients) Daily quality of life (9 patients)	Sleep quality (8 patients) Prevention of complications (4 patients)
Difficulties related with CPAP use:	Nasal obstruction (7 patients) Without any difficulties (7 patients)	Without any difficulties (9 patients) Nasal obstruction (5 patients)

Negative correlations were found in the two follow-up moments between the mean numbers of hours of CPAP use and the self-referred value in the VAS ($p<0,05$): the easier perception of use (lowest VAS values) with the longer time of CPAP utilization.

Initial values of VAS correlate inversely with adherence 1st month, and the VAS values at this point correlate inversely with long-term adherence ($p<0,05$). Statistical significant differences were found between adherence and the VAS mean value in each of two follow-up moments ($p<0,05$).

Discussion and conclusions. Before initiating CPAP treatment patients tend to under evaluate their future difficulties. The CPAP experience increases the perception of difficulties to adaptation to this treatment and its consequent abandonment in around one third of the patients. The long term run seems to bring a learning gain and with a self referred increase facility in the use of the equipment. These findings raise the issue to identify educational and training strategies at the very beginning taking into account the different sub-groups of patient's expectations.

Lack of sleep-dependent spatial memory consolidation in post-traumatic stress disorder survivors of the 2009 L'Aquila earthquake

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Objectives. Neuroimaging studies have revealed reduced volume and abnormal functional response of the hippocampi in patients with post-traumatic stress disorder (PTSD). In healthy subjects, recent neuroimaging findings showed that the hippocampus is critically involved in the formation and use of a mental representation of the environment, namely a cognitive map, and that its structural integrity affects the individual's ability to orient within the environment. Recently, we have documented that spatial performance improvement in healthy subjects occurs only when spatial learning is followed by a period of sleep. Here, we investigated whether the ability to create a cognitive map is preserved in PTSD, and whether PTSD patients exhibit a sleep effect on spatial learning as documented in healthy subjects.

Methods. The study included 11 PTSD subjects, survivors of the L'Aquila earthquake on 6 April 2009 (10 women, mean age: 22±2.7 years) and 11 healthy controls (CON, 10 women, mean age: 23±4.4 years). PTSD was diagnosed according to DSM-IV-R and all patients underwent a clinical and neuropsychological evaluation (Davidson Trauma Scale; Civilian Mississippi Scale; Emotion Attribution Task; Empathy Quotient). Participants performed a computerized 3-D virtual navigation task in which they were required to form a cognitive map of the environment (L, learning phase), followed by a retrieval task in which they were tested on the use of the cognitive map, which was tested before (test, T) and after (retest, R) one night of sleep. The time (sec) spent to form and make use of the cognitive map during test and retest was treated as dependent variable and submitted to a mixed design ANOVA with Group (PTSD, CON) as between factor and Session (L, T, R) as a repeated measure.

Results. The ANOVA showed a significant Group x Session interaction effect. Post-hoc comparisons showed that controls subjects formed the cognitive map faster than PTSD. In addition, control subjects showed a significant sleep-dependent performance improvement, an effect that was not significant in the PTSD group.

Conclusion. These findings indicate that PTSD is associated with an impaired ability to form a cognitive map of the environment, and that the well-known sleep-dependent spatial performance improvement could be not warranted in patients with PTSD. Both effects may be related to structural or functional hippocampal abnormalities.

Chronotropic parameters from cardiopulmonary exercise testing in patients with severe obstructive sleep apnea – preliminary results

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Background. Chronotropic parameters from cardiopulmonary exercise testing (CPET) have been proven to reflect autonomic dysfunction in various patient groups.

Objectives. The aim of the study is to investigate the chronotropic parameters from CPET in patients with severe obstructive sleep apnea and their contribution to the restrained physical capacity.
Methods: To the present moment 9 patients with severe obstructive sleep apnea (OSA) (age=43.9±5.6 years, body-mass index (BMI)=29.5±4.0 $kg.m^{-2}$, apnea-hypopnea index (AHI)=71.9±1.6) without known pulmonary and cardiac disease and 9 healthy controls, matched by age and body-mass index have been recruited in the study. The subjects underwent laboratory polysomnography and cardiopulmonary exercise testing on a bicycle by means of standard ramp protocol.

Results. OSA patients showed decreased physical capacity, compared to controls (VO_2/kg=21.9±4.9 vs. 28.0±2.7 $mL.kg^{-1}.min^{-1}$, p=0.04). Heart rate at rest did not differ between the investigated groups. Heart rate response (HRR=59.8±19.6 vs. 72.7±15.2 $beats.min^{-1}$) and chronotropic index (CRI=0.65±0.15 vs. 0.73±0.10) were decreased in OSA group, but statistical significance was not reached. Heart rate recovery was also slower in patients with OSA. The decrease was most pronounced at 90 sec of recovery (HRRec90=21.5±7.1 vs. 30.3±7.0 $beats.min^{-1}$, p=0.026). Heart rate recovery between 60 and 120 seconds, reflecting predominantly sympathetic function, correlated strongly and significantly with VO_2/kg in patients group (rho=0.743, p=0.035).

Conclusion. There is a trend to more pronounced chronotropic incompetence in patients with severe obstructive sleep apnea than the one that may be explained by overweight or obesity itself. Bigger studies are needed to elucidate the problem.

Spectral composition of daily light exposure in young adults in summer and winter

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Introduction. Circadian photo-entrainment is mediated in part by intrinsically photosensitive retinal ganglion cells that express the photopigment melanopsin. The spectral sensitivity of melanopsin is greatest for blue light at 480 nm. However, at present, there is little information on the time course of the spectral composition of light to which people are exposed over the 24-h period and any seasonal variation thereof.

Methods. 24 subjects aged 18-29 years, 23.8 ± 3.8 years (mean ± SD), with mean body mass index (BMI) 22.1 ± 2.3 kg/m^2 participated during the winter months (Nov-Dec), whilst 5 subjects aged 24-28 years, 27.2 ± 0.6 years, BMI 21.3 ± 0.5 kg/m^2 participated in the summer months (Apr-Jun). Subjects wore actiwatch RGB monitors (Cambridge Neurotechnology) for 7 days. These monitors measure activity, light exposure in the blue, green and red spectral regions, in addition to normal broad spectrum white light, with a two minute resolution. Subjects also completed daily sleep diaries to verify the timing of sleep and wakefulness.

Results. Analysis of the relative contribution of blue light to overall light exposure demonstrated a significant variation with time of day ($P<0.05$). Light during the 9.00-15.00h period was relatively blue light enriched (41.0 ± 0.1%, mean ± SEM), whereas during the evening during 18.00-23.00h the contribution of blue light was less (30.1 ± 1.7%). Analysis of light exposure during summer and winter demonstrated that subjects studied in summer were exposed to higher white light levels compared to those studied in winter ($P<0.002$). This difference was particularly pronounced between 15.00-20.00h. For this time interval those subjects studied in the summer were exposed to a significantly higher percentage of blue wavelength light between 16.00-20.00h, 40.2 ± 1.5% compared to winter 31.0 ± 1.2% ($P<0.05$).

Conclusions. The present data show that in addition to overall light exposure, the spectral composition of light varies with time of day and with season. These variations may contribute to inter-individual and seasonal changes in entrainment and its disorders.

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Association between lunar phase and sleep characteristics

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Objectives. There are few and contradicting results regarding the association between lunar phase and sleep, and popular belief holds that the lunar cycle affects human physiology, behavior and health. Our aim was to examine the relationship between lunar phases and sleep characteristics.

Methods. Data from 276 patients were analyzed in a cross-sectional survey, all patient had a kind of sleep disorder, but we excluded patients with apnea-hypopnea index≥15/h. Socio-demographic parameters were recorded. Data were analyzed using ANCOVA and K independent (Kruskal-Wallis) tests. All participants underwent one-night standard polysomnography, bedrooms had no window.

Results. 57% of patients were males, mean age for men was 45±14 years and 52±12 years for women. Mean sleep efficiency was 78,2%. 215 person slept during changing moon, 30 during full moon and 31 during new moon, there were no significant differences regarding age and gender between groups. Among women full moon phase was associated with lower sleep efficiency (p=0.01), shorter sleep duration (p=0.02) and REM duration (p=0.005) after adjustment for age. Self-reported fatigue in the morning (p=0.05) and self-reported time of falling asleep was higher during full moon (p=0.04). Among men the sleep duration was significantly shorter at full moon (p=0.05), while other sleep variables showed no difference across moon phases.

Conclusion. Our results support the widely held belief that sleep characteristics may vary with the moon phase, especially among women.

Differential item functioning in the Epworth Sleepiness Scale using two psychometric approaches

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Objectives. Differential item functioning (DIF) in a test means that respondents belonging to different groups (e.g. as defined by gender or age) respond differently to some items of the test even after adjusting for different levels of the property the test is designed to assess. Existence of DIF might affect the validity of a test. Epworth Sleepiness Scale (ESS) is a scale designed to assess daytime sleepiness. To our knowledge, DIF in the ESS has never been assessed. The objective was to examine whether ESS shows DIF for age or gender.

Methods. ESS data from 1168 subjects from five previous or on-going studies at our centre (61% males, age (mean+/-SD) 61.8+/-12.2 years, ESS score (mean+/-SD) 7.7+/-4.5) were analysed for DIF for gender and age (<65 yrs vs >=65 yrs) using both classical test theory (ordinal regression) and item response theory (Rasch analysis). Statistics were computed using Stata 10 (Stata Corp LP, Texas, USA) and RUMM2020 (RUMM Laboratories Pty Ltd, WA, Australia).

Results. The old group (i.e. age>65) consisted of a larger proportion of females than the young group (chi-square; $p<0.001$). Both the ordinal regression and the Rasch analysis identified statistically significant ($p<0.0005$) differential item functioning for age in items 3, 4 and 8. Significance remained after Bonferroni correction. The Rasch model also identified DIF for gender in item 3.

Conclusion. Some of the items in the ESS might have problems with differential item functioning for age. This might reflect differences in everyday activities between working and retired people, as 65 years is the standard age of retirement in Sweden. DIF for gender was only shown for item 3 in the Rasch analysis, but not in the regression model. This might be due to a somewhat higher mean age among the females than the males in our sample, meaning that the DIF ascribed to gender by the Rasch model might have been an age effect. The large group size might be a proble m as it might make even clinically unimportant DIF statistically significant.

Do you sleep regularly? – A new algorithm to determine sleep variability in sleep diaries

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Objective. An algorithm to calculate night-to-night variability of sleep is being presented based on data of sleep diaries. Sleep diaries are a common diagnostic tool in sleep medicine, especially in suspected cases of insomnia. They are also imperative in sleep research for the evaluation of (healthy) participants being either regular (and therefore “good”) sleepers or not. People with extremely irregular sleep-wake patterns prior to diagnostic polysomnography might produce artifactual results when forced to adhere to the fixed bedtimes in the sleep lab. Up to now, many authors come to the conclusion that there is no adequate way to deal with the variability in sleep diaries. Calculation of mean values, e.g. for the time of sleep onset over 14 days, is very vulnerable to distortion by outliers. Therefore, parameters like variance and standard deviation as well are not suitable measures, due to their vulnerability to be strongly influenced by outliers.

Methods. The suggested algorithm to calculate variability (R[hythm]-index) is based on i) night-to-night differences and ii) a mathematical transformation of these differences in order to minimize the impact of outliers. Calculations and a comparison of results for 50 insomnia patients who consulted our outpatient sleep disorders clinic, as well as data from 50 healthy research participants are presented.

Results. T-tests comparing patients with insomnia and good sleepers were significant (middle effect sizes) for sleep-R-index values for “sleep onset”, “morning wake up time” and “TST”. Higher R-index values for all three parameters could be documented in the insomnia group.

Conclusion. Several significant group differences between good sleepers and insomniac patients were found, however, the R-index did not allow a highly specific or sensitive diagnostic judgement. Further studies, also within the framework of the EU supported project OPTIMI (FP7-JCT-2009-4; 248544), are necessary in order to be able to determine a cut-off value for “irregular” sleep-wake patterns.

Neuroanatomical Sleep-Dependent Processing in the Probabilistic Serial Reaction Time Task

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Objectives. This fMRI study investigates sleep-dependent changes in neuroanatomical activity during probabilistic sequence learning.

Methods. Twenty-five healthy young adults performed a 6-choice probabilistic serial reaction time (SRT) task. Unknown to them, the sequential structure of the stimuli was based on a finite-state grammar. To assess learning, there was a 15% chance on each trial of replacing the grammatical (G) with a non-grammatical (NG), random stimulus. Three sessions (24 blocks, 65 trials each) were administered in the fMRI environment, two at day 1 and one at day 4, at the same time of day. During the first post-training night, 12 subjects sleep regularly (RS) while 13 others were sleep deprived (SD) under controlled conditions. Functional volumes were acquired using an EPI sequence (3 Tesla Siemens Allegra), spatially transformed and analyzed using SPM8b and a random effect model.

Results. Contextual sensitivity gradually emerged through practice with higher mean RTs (per block) for NG than G stimuli. Analysis of behavioral data disclosed main effects of Session and Grammatically (ps <.001) only. Despite same behavioral effects in RS and SD groups, analysis of fMRI data using canonical hemodynamic responses and their temporal derivatives showed that NG event-related BOLD responses differ between groups in a sleep-dependent manner. For the SD group, NG stimuli elicited slower onset activations (ps^{corr} <.05) in the left fusiform gyrus [-30.0 -64.0 -6.0], the superior parietal lobule/right cuneus [4.0 -82.0 40.0] and the right inferior frontal area [44.0 10.0 20.0].

Conclusions. Although subjects performed the SRT task in a similar manner whether sleep deprived or not on the first posttraining night, onset differences in hemodynamic response between G and NG items are attenuated in the RS but not SD condition, suggesting that posttraining sleep favours the successful integration (and/or a faster detection) of deviant stimuli at the cortical level.

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The role of personality traits in insomnia

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Objectives. Insomnia is a highly prevalent sleep disorder, known to affect psychological well-being and quality of life. While perpetuating factors have received much attention, the role of predisposing factors has not been studied in much detail. The susceptibility to develop insomnia may be linked to the presence of certain personality features. Here, we review studies that assessed this particular aspect of insomnia.

Methods. Pubmed was searched up to July 2009, using a combination of both MeSH terms and free text words. We screened the abstracts of the papers found, to retrieve those research articles that specifically dealt with the topic of insomnia and personality. Only articles in which personality traits were measured with self-report questionnaires were selected. Although there are various clinical classification systems that cover insomnia, in many studies classification criteria were either unofficial or not mentioned. We decided not to exclude these studies in our present. Eventually, we retrieved the full manuscript from 38 articles that contained relevant information for the reviewed topic.

Results and conclusion. Due to various methodological issues, definitive conclusions cannot be drawn as of yet, and several conflicting findings remain. However, there is a common trend indicating that insomniacs display more signs of ‘neuroticism’, ‘internalization’, anxious concerns and traits associated with perfectionism. These factors may play varying roles depending on the specific subdiagnosis of insomnia. In addition, certain personality traits may be related to the response to (cognitive) behavioral treatment. For instance, insomniacs reporting less ‘guardedness’ and have a higher score on the MMPI ‘hypomania’-scale show less improvement through psychological treatment. The specific role of personality traits in the etiology insomnia is not yet clear, because of a lack of longitudinal data. Personality factors may play a causal role in the development of insomnia, but may also be a consequence of the sleep problem and the associated daytime dysfunction. Future longitudinal studies should not view personality as a single predisposing factor, but assess it as a part of a larger group of interacting psychological and physiological factors involved in the predisposition to and perpetuation of chronic insomnia.

Non-invasive measurements of respiratory effort

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Objectives. The diagnosis of sleep-related breathing disorders (SRBD) is based on the registration of obstructed breathing events during sleep. These events may include obstructive apneas, hypopneas or respiratory effort-related arousals.
The reference method for measuring respiratory effort and to differentiate between obstructive and central events is esophageal pressure monitoring (Pes).
Pes is often uncomfortable for the patients and difficult to incorporate into routine sleep studies.
Alternative non-invasive techniques to measure respiratory effort are therefore needed. In this study, we review studies comparing alternative non-invasive techniques to Pes. The list of non-invasive techniques we have included is: pulse transit time (PTT), respiratory inductive plethysmography (RIP), nasal pressure (NP), suprasternal pressure (Pst), diaphragm electromyography (EMGdi), crescendo snoring, midsaggital jaw movement (JAWAC).

Methods. Pubmed and Cochrane Central Register was searched up to October 2009, using a combination of both MeSH terms and free text. First, all papers dealing with SRBD and one of the non-invasive techniques were identified. Second, articles in which a non-invasive technique was compared to Pes were selected. Eventually, 19 articles were eligible for this study.

Results and conclusions. Definite conclusions can not be drawn, because of various methodological issues. However, PTT and Pst seem promising alternative non-invasive techniques. No data were found about JAWAC. Extensive research have been done yet to find the best non-invasive technique or the best combination of non-invasive techniques to measure respiratory effort.

Restless legs syndrome in patients with multiple sclerosis: epidemiology and genetics

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Objectives. The restless legs syndrome (RLS) is a frequent neurological disorder and it presents as both idiopathic and secondary from. Idopathic RLS is associated with common genetic variants in *MEIS1, BTBD9*, *PTPRD* and *MAP2K5/LBXCOR1*. Recently, multiple sclerosis (MS) was indentified as common cause for secondary RLS, the prevalence of RLS in MS patients ranges from 13.3 to 37.5.%. The aim of our study was to evaluate the prevalence of RLS among the Czech patients with MS and to further analyze the impact of known genetic determinants for RLS in patients with MS.

Methods.
Epidemiological study: We enrolled consecutively Czech patients with multiple sclerosis coming to our center. Each patient underwent a semistructured interview. A patient was considered to be affected by RLS if he/she met all four standard criteria at life long interval.
Genetic study: In the genetic association study, 642 subjects were included, 203 MS patients with RLS were compared to 438 MS patients without RLS. In total 13 single nucleotide polymorphisms within the four genomic regions were genotyped according to the results of previous genome-wide association scans using mass spectrometry .

Results.
Epidemiological study: A total of 765 subjects (553 females, 211 males, mean age 36.54, ±SD 9.5) with multiple sclerosis were included in the study. The diagnosis of RLS was confirmed in 245 subjects (32.1%, 95% CI 28.7-35.4%) with MS. Patients suffering from both MS and RLS were significantly older (38.6 vs. 35.6 years), had longer durations of MS symptoms (11.0 vs. 8.2 years) and had higher EDSS score (2.9 vs. 2.3).
Genetic study: No significant association with *MEIS 1*, *BTBD9* and *PTPRD* was found in 203 patients with multiple sclerosis, despite sufficient statistical power for first two loci. There was a trend for association with *MAP2K5/LBXCOR1* - the best model for the risk allele was the recessive model (p nominal = 0.0029, p corrected for four loci and allelic + recessive model = 0.023, odds ratio = 1.60 - 95% CI 1.17 – 2.18).

Conclusion. We confirmed the findings of previous studies that life long RLS prevalence is high in patients with multiple sclerosis. MS should be considered among causes of secondary RLS forms. The genetic risk variants *MEIS 1* and *BTBD9* for idiopathic RLS do not increase the risk for the secondary RLS in MS, *LBXCOR 1* can partially contribute to the phenotype. In patients with MS, RLS may be the consequence of specific lesion of central nervous systems pathways involved in the aetiology RLS.

Determinants of REM sleep without atonia in narcolepsy-cataplexy

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Objectives. REM sleep dysregulation has been frequently reported in Narcolepsy-Cataplexy (NC) with mainly a loss of muscular atonia during REM sleep periods. However the determinants of this atonia remained unclear. Our aim was to characterize the determinants of REM dissociated events and of clinical REM behaviour disorder (RBD) in NC.

Patients and Methods. Polysomnographic recordings of 65 NC (39 men/26 women, ages ranged 10-85 years) free of drugs for at least 15 days were consecutively analyzed. REM sleep features were scored with the quantification of tonic (duration above 20% of REM sleep time) and phasic muscular activity (duration above 15% of REM sleep time) in submentalis muscle, rapid eye movements density and periodic limb movements index in REM sleep. We collected clinical data of NC patients: age, sex, age of onset, and presence of clinical RBD.

Results. 27 of the 65 patients (41%) presented a clinical RBD. 21 of 27 (77%) NC with clinical RBD were men and 12 of them (44%) were aged above 50 years. Mean age at onset of NC in the RBD group was 25.6 y.o. and 18.8 y.o. in absence of RBD. There were no between-group difference between the index of tonic EMG activity, index of phasic EMG activity, rapid eye movements density, and PLM index during REM sleep. In addition, we failed to report any age effect in the amount of REM dissociated sleep events but tonic and phasic muscular activities trended to be greater in patients with later age at onset.

Conclusion. REM sleep without atonia is a frequent polysomnographic finding in NC but without any association with a positive clinical history of RBD. Our results suggest that REM sleep dissociation and clinical RBD had different pathogenic processes in NC. As in idiopathic RBD there is a male predominance in NC with clinical RBD. Finally, age *per se* was not a determinant for dissociated REM sleep but higher motor activities were reported in patients with later age of the condition.

Sleep and EEG effects of gamma-hydroxybutyrate, baclofen and GABAB receptor subunits

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Objectives. Gamma-hydroxybutyrate (GHB), the only drug approved to treat the sleep disorder narcolepsy, targets GABAB receptors. These receptors are heterodimers composed by the GABAB2 subunit and either one of the two GABAB1 subunit isoforms 1a and 1b. The mechanism of action of GHB and the role of GABAB receptors in sleep is still poorly understood. Thus, we investigated the effects of GABAB receptors, GHB and baclofen (BAC), a high affinity GABAB receptor agonist, on electroencephalogram (EEG) and sleep.

Methods. We performed EEG recordings in mice lacking functional GABAB receptors (1-/- and 2-/-) or lacking one of the subunit 1 isoforms (1a-/- or 1b-/-) and evaluated sleep and EEG effects in baseline conditions and after the administration of the GHB-prodrug, gamma-butyrolactone (GBL), and BAC.

Results. We discovered that the distribution of sleep over the day was profoundly altered in 1-/- and 2-/- mice suggesting a major role for GABAB receptors in circadian phase-setting. For several other sleep and EEG variables 1a-/- mice were intermediate between 1-/- and 2-/- mice, on the one hand, and 1b-/- and WT mice on the other, pointing to a more prominent role of the 1a isoform. Moreover, we found that this isoform protects against the spontaneous seizure activity observed in 1a-/-, 1-/-, 2-/- mice. GBL induced an anesthetic-like state distinct from physiological sleep, which did not affect subsequent sleep. In contrast, BAC increased sleep need reminiscent of sleep-deprivation-induced hypersomnia. These effects of both drugs were completely lost in 1-/- or 2-/- mice suggesting GABAB receptors as their unique targets. Nevertheless, the effects of GBL and BAC differed, likely due to their different GABAB binding affinities.

Conclusion. A lack of GABAB receptor subunit leads to an altered sleep distribution over 24h baseline conditions. The isoform 1a protects against the development of spontaneous epileptiform phenotype. Behavioral changes induced by GHB via GABAB receptors differ from sleep and are compatible with anesthetic state. Furthermore, GHB does not affect sleep regulation and hypersomnia while BAC does.

Cardiovascular responses in preterm infants at 34 – 39 weeks of conceptual age

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Objectives. Only a few studies have evaluated acute cardiovascular control in preterm infants with continuous blood pressure (BP) measurement. Baroreflex control in premature infants appears to be properly developed shortly after birth. Full-term, 3-month-old infants show consistently biphasic heart rate (HR) responses to postural challenges, with an initial increase followed by a decrease and a return to previous HR level. However, BP responses in these infants are characterized with a large qualitative and quantitative intersubject variability.

Methods. We studied twenty preterm infants with a mean gestational age of 31 ± 2.4 (26 – 34) wk at birth at the conceptual age of 36 ± 1.5 (34 – 39) wk. 45° head-up tilt and side motion tests, HR variability, and HR responses to spontaneous arousals were evaluated in quiet non-REM sleep. Results were compared to previously reported results of twenty, healthy, full-term control infants studied at the age of 12 ± 3 weeks.

Results. Preterm infants showed significantly smaller initial HR and BP responses compared to controls in both head-up tilt (HR $P = 0.0005$, systolic BP $P = 0.02$, diastolic BP $P = 0.01$) and side motion tests (HR $P = 0.002$, systolic BP $P < 0.0001$, diastolic BP $P < 0.0001$). Furthermore, in tilt tests, preterm infants presented with greater intersubject variability in BP responses than controls (SBP $P = 0.009$, DBP $P = 0005$). HR responses to spontaneous arousals in preterm infants were similar to those of the control infants.

Conclusion. This study found that preterm infants show highly variable BP response and a flat HR response to head-up tilt test suggesting more labile acute BP control to postural challenge compared with older infants or adults.

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Sleep, daily PER2 expression and melatonin secretion levels: findings from patients and healthy controls

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Objectives. To assess circadian rhythmicity using sleep diary, gene expression and endocrine markers both in healthy adults and in patients suffering from depression or type 2 diabetes.

Methods. Fourteen individuals (sex ratio 1:1), aged 28-65 (mean age: 51.6±12.3), self-selected from a larger sample that was genotyped for a PER3 VNTR, completed a sleep diary for ten days, as well as a questionnaire assessing diurnal preference, subjective sleep quality and depression, and donated biological samples (buccal swabs and saliva) every four hours over a 24 hours period. Quantitative PCR was carried out to measure gene expression in buccal samples and relative expression levels of the circadian clock gene PER2 were examined. Salivary levels of melatonin were determined by ELISA.

Results. Patients displayed more disturbed sleep compared to controls. Daily melatonin secretion curve was more dampened in diabetics To date, six individuals had their PER2 expression profile determined, with preliminary findings indicating altered rhythms in depression and diabetes.

Conclusions. These preliminary results provide novel evidence circadian rhythms are disturbed both at molecular and behavioural levels in depression and diabetes.

Serum levels of MMP-9, sRAGE, hsCRP and Cu can be used as predictive biochemical parameters related to oxidative stress in obese patients with obstructive sleep apnea

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Objectives. Obstructive sleep apnea (OSA) is one of many conditions contributing to oxidative stress. The aim of the study was to ascertain if there is any connection between OSA and its severity and novel oxidative stress related markers. Matrix Metalloproteinases 2 and 9 (MMP-2, MMP-9), high sensitive C-reactive protein (hsCRP), Pregnancy Associated Plasma Protein-A (PAPP-A), soluble Receptors for Advanced Glycation End-products (sRAGE), zinc (Zn) and copper (Cu) were measured. Further biochemical markers were also evaluated (fibrinogen, standard biochemical markers and blood count).

Methods. 51 men suspected for OSA indicated for night polygraphy were included in the study. Ventilation parameters were measured: apnea/hypopnea index (AHI), oxygen desaturation index (ODI), mean blood hemoglobin oxygen saturation (SpO2) and time of blood hemoglobin oxygen saturation below 90% (SpO2<90%). Morning venous blood samples were taken.

Results. We found strong positive correlation between BMI and levels of Cu, MMP-9, hsCRP, fibrinogen, and negative correlation BMI with sRAGE. From ventilation parameters we found positive correlation of ODI and SpO2<90% with markers MMP-9 and hsCRP. sRAGE level correlated with AHI and ODI negatively. SpO2 correlated negatively with Cu, MMP-9, hsCRP and fibrinogen. There was no correlation between ventilation parameters and markers MMP-2, PAPP-A and Zn. Compared to severity of OSA there was significant difference in levels of hsCRP and Cu between patients with AHI ≤ 5 and AHI ≥30 independently to BMI.

Conclusions. Obstructive sleep apnea can participate as one of many conditions for oxidative stress state in the body. MMP-9, hsCRP, sRAGE and Cu seem to be strong predictors of oxidative stress in OSA patients. Strong correlation between oxidative stress related markers and OSA is elucidated by connection of these to BMI and BMI is probably primary condition of oxidative stress.

Key words: obstructive sleep apnea, oxidative stress, MMP-9, MMP-2, sRAGE, hsCRP, Cu, Zn, PAPP-A

Effect of total sleep deprivation on endothelial function and heart rate variability in shift workers and non-shift workers

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Objectives. Endothelial dysfunction, alterations in heart rate variability (HRV) (a lower variance and higher sympathetic activity), shift work and sleep deprivation have been associated with an increased risk for cardiovascular disease. The aim of the current study was to investigate the effect of one night of total sleep deprivation (TSD), a recovery nap and recovery sleep on endothelial function and HRV and to compare shift workers and non-shift workers in controlled laboratory conditions.

Methods. Eleven experienced shift workers (shift work ≥ 5 years) and 14 non-shift workers were matched for age, body mass index and cholesterol. Endothelial function as % flow-mediated dilatation (FMD) was assessed by ultrasound twice a day. HRV parameters derived from polysomnographic electrocardiograms were determined five times a day (variance calculated by the standard deviation of normal-to-normal interval (SDNN) and sympathetic/parasympathetic balance reflected by the low frequency/high frequency ratio (LF/HF)). Both HRV and FMD were assessed following adaptation sleep, baseline sleep, TSD and recovery sleep (body posture, food intake and light controlled throughout).

Results. A trend (P=0.07) for a lower %FMD (lower endothelial function) in shift workers was observed, likely due to a decreased %FMD after TSD. There was a significant effect of group on SDNN ($F_{1,430}$=15.1, P<0.001), showing significantly lower SDNN in shift workers compared to non-shift workers (P<0.001) and a significant day*time interaction ($F_{12,430}$=2, P<0.05), most consistently revealing higher SDNN 15 min after habitual wake up time following TSD (P<0.01). Furthermore, LF/HF showed significant effects of group ($F_{1,417}$=4.2, P<0.05), day ($F_{3,417}$=5.4, P<0.01) and time ($F_{4,417}$=12.7, P<0.001). LF/HF was significantly higher in shift workers than in non-shift workers (P<0.05) and significantly higher after baseline sleep, TSD (P<0.01) and recovery sleep (P<0.001) compared to adaptation sleep.

Conclusion. In agreement with previous studies, an increased SDNN peak around habitual wake up time after sleep deprivation was observed. How this higher SDNN relates to sleep deprivation is not clear. In shift workers the significantly higher LF/HF reflects higher sympathetic activity and the significantly lower SDNN indicates lower heart rate variability. In conclusion, alterations in HRV in shift workers, assessed non-invasively, may, in part, contribute to their increased risk for cardiovascular disease.

Is the temperature in your bed related to sleep onset?

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Objectives. Sleep onset latency is related to the rise is skin temperature and the drop in core body temperature. This rise in skin temperature might be hampered by entering a relatively cool bed that might result in a vasoconstriction of the skin and hence drop in skin temperature. We measured the gradual increase of the near skin temperature in the bed and explored if it was correlated to the sleep onset latency.

Methods. 17 subjects without sleep complaints participated in the study, main age was 33 years. Subjects were monitored for 2 nights in their home environment and they were advised to go to bed at habitual bed time. Sleep was monitored using a frontal EEG-EMG-EOG based sleep monitor (Zeo Inc, USA). Sleep onset was based on the Time to Z output of the ZEO system, reflecting time to fall asleep. Temperature in bed was monitored using 16 Ibuttons (DS1923; Maxim/Dallas Semiconductor Corp, USA) equally distributed on the inside of a duvet cover. For preliminary analyses we selected the data of the 4 central Ibuttons (near trunk of the body) and the 2 lower central Ibuttons (near the feet). Temperature in the bed just before entering the bed and the steady temperature after the initial rise were determined. The change of the temperature in bed was quantified by time to warm up the bed, increase in bed temperature and speed of bed warming.

Results. Time to fall asleep was negatively affected by with the time to warm up the bed. The faster the increase of the bed temperature near the feet, the shorter it takes to fall asleep (p =< .05). Changes in temperature near the trunk of the body did not significantly affect sleep onset. The effect of the initial temperature in the bed near the trunk (warmer bed associated with shorter sleep latencies) only reached trend level. No other effects could be observed.

Conclusions. The rate of change in the bed temperature at the feet area is caused by the temperature of the feet, warming up that particular bed area. Our observation is in line with previous results showing that faster increases of foot temperature after lights-off seemed to be involved in shortening sleep onset latency, suggesting a role for the rate of change rather than the level of distal temperature.

REM sleep behavior disorder in narcolepsy

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Objectives. Narcolepsy is a hypersomnia of central origin, characterized by excessive daytime sleepiness, cataplexy, sleep paralysis and hypnagogic hallucinations. Recent studies showed higher incidence of REM sleep behavior disorder (RBD) in narcolepsy than it has been estimated previously. Therefore we evaluated the incidence of RBD in consecutive patients with narcolepsy referred to our sleep disorders center.

Methods. Within the group of patients examined because of hypersomnia, diagnosis of narcolepsy was established in 38 patients (mean age 35.3 □ 14.1; 15 females, 23 males) on the basis of clinical features, polysomnography (PSG) and Multiple Sleep Latency Test (MSLT). Video-PSG recordings were reviewed for presence of increased muscle tone recorded from chin and tibialis anterior muscles with or without visible motor activity during REM periods, manifested as excessive, violent body movements (especially legs) and/or vocalization. All newly diagnosed patients as well as those reporting to follow-up visits were questioned about symptoms suggesting RBD. For statistical analysis Mann-Whitney U-test and Fisher exact test were used.

Results. We found clinical and/or polysomnographical features of RBD in 36,8% of investigated patients. Symptomatic and polysomnographically documented RBD was found in six patients. Disturbances of muscle tone regulation during REM sleep without clinical symptoms were found in PSG in another four patients. Among patients reporting to follow-up visit four subjects confirmed clinical symptoms corresponding RBD of various severity.

Conclusions. Our findings are consistent with recently published studies, suggesting stronger relationship between narcolepsy and RBD than it has been observed previously. Questions related to the symptoms of RBD, that may be injurious for the patient or patient's bed partner, should be routinely asked to every patient with narcolepsy.

The influence of pre-sleep cognitive arousal on sleep onset processes

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Objectives. Cognitive hyperarousal, resulting in enhanced cognitive activation (CA), has been put forward as an important factor in the development and preservation of insomnia. In an attempt to develop a valid experimental model of insomnia this study examined the effects of acutely induced pre-sleep cognitive hyperarousal on sleep onset (SO) processes.

Methods. Following an adaptation night 20 subjects (age between 19 and 50 years, 26,45 years +/- 8,61) slept two nights in the sleep lab after an evening reference (RE) and cognitive activation (CA) condition. This was executed in a counterbalanced order. In the CAcondition subjects worked themselves through half an hour of intense cognitive tasks (Digit Span Forward, two versions of Stroop-tasks, a memory recognition task and the Symbol Substitution task) prior to retiring for bed. SO was defined as the latency from lights out to the first stage 1 epoch according the Rechtschaffen and Kales (1968) criteria. In addition the skin temperature was monitored at the right axilla as an index of heat loss.

Results. The induction of a cognitive load was successful (z = 2,52; *p* = 0,01; N = 18), as it resulted in higher subjective scores on a visual analog scale post (1,21 +/-1,72) as compared to prior the tasks (0,29 +/-0,83). This was not observed in the RE-condition. Physiologically the heart rate (HR) at and during SO was significantly higher (z = 4,55; *p* = 0,00; N = 12) in the CA-condition (68,00 bpm +/- 4,48) as compared to the Recondition (62,18 bpm +/- 2,02) and after sleep onset the HR in the CA-condition (62,28 +/- 2,83) stayed significantly higher (z = 4,36; *p* = 0,00; N = 12) for at least the first 15 minutes compared to the RE-condition (59,56 +/- 0,94). Objective SO-latency was significantly prolonged (z = 2,59; *p* = 0,01; N = 12) in the CA-condition (13,42 min +/- 6,54) compared to the RE-condition (8,75 min +/-4,94). It is well known that during SO temperature at the axilla (axilla-T) increases to release body heat and to promote sleep. Although axilla-T during SO was significantly lower (z = 3,92; *p* = 0,00; N = 12) in the CA-condition (36,42 C° +/-0, 33) as compared to the RE-condition (36,90 C° +/-0,22), after SO the a xilla-T of the CO-condition (37,57 +/- 0,20) was significantly higher (z = 8,15; *p* = 0,00; N = 12) during the first 45 minutes compared to the RE-condition (37,42 +/- 0,18).

Conclusion. Pre-sleep cognitive activation induced a significant cognitive load in our subjects. It lengthened subsequent sleep onset latency and furthermore it interfered with the HR and the axilla-T during the first hour of time in bed. These results suggest a mediating role of heart rate and temperature in sleep onset problems and warrant further research on interventions to influence sleep onset processes in acute and chronic insomnia.

Dynamic changes in neurotransmitter levels in the basal forebrain during and after sleep deprivation

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Objectives. The basal forebrain (BF) participates in the control of vigilance state through its cortical cholinergic, GABAergic and glutamatergic projections and receives projections from all major wake-inducing neurotransmitter systems, including the cholinergic, noradrenergic, histaminergic and serotonergic systems. The firing rate of the wake-promoting neurons in the BF is decreased by adenosine, an inhibitory neuromodulator. Adenosine levels increase and promote sleep during sleep deprivation (SD). However, the animals are able to stay awake, suggesting increased activity of the wakefulness-maintaining systems to counteract the effect of sleep pressure.

Methods. Male Han-Wistar rats were subjected to a 6h SD by 'gentle handling'. In vivo microdialysis was used to sample the BF extra cellular space. Samples for neurotransmitter measurement were collected before, during and after SD and analysed using HPLC/RIA.

Results. The concentrations of 5-hydroxyindoleacetic acid (5-HIAA, the main metabolite of serotonin), homovanillic acid (HVA, a major metabolite of dopamine) and dopac (a major metabolite of dopamine) increased during SD, reaching a plateau after 3 hours and decreased to baseline during recovery sleep. Corticosterone levels were elevated after 4 hours of SD, however, they never increased above normal circadian peak levels. Histamine levels increased significantly immediately after starting SD, remaining above baseline levels throughout SD, histamine levels returned back to baseline concentrations as soon as SD was terminated.

Conclusions. Monoamine levels gradually increase during SD, reaching a plateau after 3 hours, suggesting increased activity of the ascending arousal systems to counteract the effect of enhanced sleep pressure. Corticosterone levels stay at baseline for the first 3 hours of SD, the increase during the last 3 hours of SD does not exceed the circadian peak. Histamine levels appear to be unaffected by increased sleep pressure and reflect different vigilance states.

Sleep disturbance impedes stroke recovery in the rat

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Introduction. Sleep disturbance (SDis) represents a risk factor for stroke recovery. We have previously showed that SDis over 3 days aggravates brain damage in rats subjected to focal cerebral ischemia. The aim of this study is to further investigate the effects of SDis on long term stroke recovery.

Methods. Focal cerebral ischemia was induced by occlusion of the distal branches of Middle Cerebral Artery (MCAo). 12 hours after ischemia, one group of rats (n=9) was subjected to SDis (12h of sleep deprivation over 3 days) by gentle handling and another group (n= 8) left undisturbed (w/o SDis). Sham-operated animals were also assigned to either SDis (n=6) or left undisturbed (n=6). Rats were allowed to survive for 5 weeks after surgery. Single Pellet Reaching test (SPR) was used for assessing sensorimotor function, Nissl staining for infarct size, biotinylated dextran amine (BDA) tracing for axonal sprouting and bromo-desoxyuridine (BrdU) staining for neurogenesis.

Results. After MCAo the SPR performance dropped to 4 % of baseline (100%). At day 35 the recovery in the SDis group was less than 50% whereas in the w/o SDis group was almost complete. Repeated measures ANOVA indicated a significant difference ($p = 0.001$) in group*time interaction ($F(12, 101) = 11$). Independent t-tests showed significant difference at day 14 (w/o SDis 45%±17 vs. SDis 19%±25, $p=0.031$), 21 (w/o SDis 55%±26 vs. SDis 21%±21, $p=0.008$), 28 (w/o SDis 50%±24 vs. SDis 25%±24, $p=0.045$) and 35 (w/o SDis 71%±30 vs. SDis 38%±34, $p=0.052$). There was significant increase ($p=0.035$) in the damage area in the SDis group (18%±4.3) compared with the w/o SDis group (11%±4.5). The BDA stained area in the contralateral motor cortex and striatum was significantly smaller ($p<0.05$) in the SDis than in the w/o SDis group. Furthermore there was significant ($p=0.01$) decrease in the number of BrdU positive cells in the peri-infarct area in the SDis group (50±20cells/section) compared with the w/o SDis group (141±36cells/section). Double staining showed that in both groups about 70% of BrdU stained cells were associated with a neuronal marker (NeuN) and about 30% with the endothelial marker Von Willebrand factor.

Conclusion. Sleep disturbance over 3 days has a significant detrimental effect on stroke recovery. It reduces ischemia-related axonal sprouting, neurogenesis and angiogenesis.