

SCIENTIFIC PROGRAM

Thursday, June 11, 2009

SCHEDULE AT A GLANCE

Thursday, June 11, 2009

Symposia	8:00am – 10:00am
Oral Presentations	8:00am – 10:00am
Refreshment Break	10:00am – 10:15am
Symposia	10:15am – 12:15pm
Oral Presentations	10:15am – 12:15pm
Late Breaking Abstracts	10:15am – 12:15pm

SYMPOSIA

8:00am – 10:00am

S 22: Sleep and Hypertension

8:00am – 10:00am

Ballroom 6C

Chair: Antonio Culebras, MD, FAASM

Faculty: Shahrokh Javaheri, MD, FAASM; Clete Kushida, MD, PhD, RPSGT, FAASM; Jacques Montplaisir, MD, PhD; Virend Somers, MBChB, PhD

- 8:00am - 8:05am **Introduction: Sleep and Vascular Disease**
Antonio Culebras, MD, FAASM
- 8:05am - 8:30am **Apnea, the Arousal Response and Hypertension**
Virend Somers, MBChB, PhD
- 8:30am - 9:00am **Sleep Apnea and Hypertension: A Clinical Perspective**
Clete Kushida, MD, PhD, RPSGT, FAASM
- 9:00am - 9:30am **Restless Legs Syndrome, Periodic Limb Movements and Hypertension**
Jacques Montplaisir, MD, PhD
- 9:30am - 10:00am **Short Sleep and Elevated Blood Pressure**
Shahrokh Javaheri, MD, FAASM

Objectives:

1. Describe the intimate relationship between sleep, sleep disorders and high blood pressure.
2. Discuss the relationship between sleep apnea, periodic limb movements, insomnia and poor sleep quality with high blood pressure.
3. Discuss how to manage patients with high blood pressure through identification of sleep disorders that raise blood pressure.

S 23: Does Sleep Have a Universal Vital Function across Individuals and Species

8:00am – 10:00am

Rooms 606-609

Chair: Jerome Siegel, PhD

Faculty: Chiara Cirelli, MD, PhD; David Dinges, PhD; Amita Sehgal, PhD

- 8:00am - 8:30am **The Need for Sleep in *Drosophila***
Amita Sehgal, PhD
- 8:30am - 9:00am **Is Sleep Essential? Insights from Flies and Rodents**
Chiara Cirelli, MD, PhD
- 9:00am - 9:30am **What does Modern Human Sleep Need and Response to Sleep Loss Suggest regarding a Universal Function for Sleep?**
David Dinges, PhD
- 9:30am - 10:00am **Sleep as a State of Adaptive Inactivity**
Jerome Siegel, PhD

Objectives:

1. Explain the variability of sleep duration and quality between various species.
2. Describe the variation between humans in sleep duration and quality and response to sleep deprivation.
3. Discuss these phenomena in the context of possible functions of sleep.

S 24: Making Decisions while Sleep Deprived: Caveat Emptor

8:00am – 10:00am

Ballroom 6B

Chair: Sean Drummond, PhD

Faculty: Michael Chee, MBBS; David Dickinson, PhD; William Killgore, PhD

- 8:00am - 8:30am **Betting Your House on a Sleep Deprived Brain - The fMRI Evidence**
Michael Chee, MBBS
- 8:30am - 9:00am **Sleep Deprivation and Emotional Decision-making**
William Killgore, PhD
- 9:00am - 9:30am **Effects of Total and Partial Sleep Deprivation on Decision-making: Behavior and Brain Function**
Sean Drummond, PhD

SCIENTIFIC PROGRAM

Thursday, June 11, 2009

9:30am - 10:00am **The Effects of Naturally-occurring Sleep Loss and Circadian Mismatch on Decision Dynamics**
David Dickinson, PhD

Objectives:

1. Explain the multitude of contexts and scenarios covered by the term “decision-making.”
2. Discuss the behavioral effects of sleep deprivation and sleep restriction on various aspects of decision-making.
3. Review the neural effects of sleep deprivation on various aspects of decision making as measured with functional magnetic resonance imaging (fMRI).

ORAL PRESENTATIONS

8:00am – 10:00am

Authors selected for oral presentations are allotted a 10-minute time period to present their abstract, followed by a 5-minute time period for questions and answers. The four-digit abstract number corresponds to the abstract book.

19: Epidemiological Correlates of SRBD

8:00am – 10:00am

Ballroom 6A

Chair: Sanjay Patel, MD

Objective: Review causes and consequences of obstructive sleep apnea as elucidated by epidemiological studies.

#0502 8:00am - 8:15am
PREVALENCE OF OBSTRUCTIVE SLEEP APNEA SYNDROME IN SAO PAULO EPIDEMIOLOGICAL SLEEP STUDY
Tufik S, Santos-Silva R, Taddei J, Bittencourt L

#0504 8:15am - 8:30am
CANDIDATE GENE ANALYSIS FOR OBSTRUCTIVE SLEEP APNEA
Patel S, Larkin E, Goodloe R, Li Y, Adams M, Redline S

#0503 8:30am - 8:45am
REVERSE CAUSALITY IN THE ASSOCIATION OF SLEEP-DISORDERED BREATHING AND CARDIOVASCULAR DISEASE
Chami H, Resnick H, Quan S, Gottlieb D

#0500 8:45am - 9:00am
RECIPROCAL INTERACTIONS OF OBSTRUCTIVE SLEEP APNEA AND HYPERTENSION WITH ACE I/D POLYMORPHISM IN MALES
Koyama R, Drager L, Lorenzi-Filho G, Cintra F, Pereira A, Poyares D, Krieger J, Tufik S, de Mello M, Pedrazzoli M

#0505 9:00am - 9:15am
ROLE OF OBESITY ON SLEEP BREATHING DISORDER NOT ASSOCIATED WITH OSA
Palombini L, Tufik S, Guillemineault C, Silva R, Bittencourt L

#0515 9:15am - 9:30am
SLEEP-DISORDERED BREATHING AND WEIGHT GAIN: THE SLEEP HEART HEALTH STUDY
Brown M, Goodwin J, Silva G, Behari A, Newman A, Punjabi N, Resnick H, Robbins J, Quan S

#0498 9:30am - 9:45am
THE ASSOCIATION BETWEEN OBSTRUCTIVE SLEEP APNEA AND NEONATAL BIRTHWEIGHT
Louis J, Redline S, Auckley D

#0509 9:45am - 10:00am
SLEEP DURATION AND CARDIOVASCULAR CONSEQUENCES IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA
Cintra F, Riso T, Poyares D, Oliveira W, Tufik S

20: Sleep in Mood Anxiety and Substance Abuse Disorders

8:00am – 10:00am

Rooms 611-614

Chair: Anne Germain, PhD

Objective: Evaluate sleep disturbance in patients with psychiatric disorders.

#1057 8:00am - 8:15am
ALPHA-DELTA SLEEP IN MAJOR DEPRESSIVE DISORDER
Jaimchariyatam N, Kirkwood K, Budur K

#1054 8:15am - 8:30am
SLEEP MISPERCEPTION AMONG OLDER ADULTS WITH PAIN, DEPRESSION, OR SLEEP COMPLAINTS
Kay D, McCrae C, Rowe M

#1059 8:30am - 8:45am
PHASE RELATIONSHIPS BETWEEN CORE BODY TEMPERATURE, MELATONIN, AND SLEEP ARE ASSOCIATED WITH DEPRESSION SEVERITY: PRELIMINARY EVIDENCE FOR CIRCADIAN MISALIGNMENT IN NON-SEASONAL DEPRESSION
Hasler B, Buysse D, Kupfer D, Germain A

THURSDAY

SCIENTIFIC PROGRAM

Thursday, June 11, 2009

- #1055** 8:45am - 9:00am
COMPARISON OF PRE-SLEEP WAKING QEEG IN VETERANS WITH PTSD, ADULTS WITH PRIMARY INSOMNIA, AND GOOD SLEEPERS
Jennifer A, Walsh C, Cashmere D, Seres R, Miewald J, Buysse D, Germain A
- #1056** 9:00am - 9:15am
STABILIZING SLEEP AND DAILY ROUTINE IN VETERANS WITH COMORBID PTSD AND DEPRESSION: FOLLOW-UP OUTCOMES FOR COGNITIVE BEHAVIORAL SOCIAL RHYTHM THERAPY
Haynes P, Kelly M, Scheller V, Quan S, Bootzin R
- #1060** 9:15am - 9:30am
ACTIGRAPHIC COMPARISON OF SLEEP IN COMORBID POSTTRAUMATIC STRESS DISORDER AND DEPRESSION VERSUS DEPRESSION ALONE
Kelly M, Bootzin R, Ancoli-Israel S, Haynes P
- #1058** 9:30am - 9:45am
ACUTE SLEEP DEPRIVATION AND PANIC VULNERABILITY: EXAMINING THE ROLE OF ANXIETY SENSITIVITY
Babson K, Feldner M
- #1061** 9:45am - 10:00am
THE IMPACT OF ALCOHOLISM IN MEN AND WOMEN ON POLYSOMNOGRAPHY AND SLEEP EEG
Colrain I, Wagstaff A, Mayer B, Hoffman L, Turlington S, Baker F
- 21: Sleep and Medical Disorders**
8:00am - 10:00am
Ballroom 6E
Chair: David Bradshaw, MD, FAASM
Objective: Evaluate sleep disturbance in patients with medical disorders and chronic pain syndromes.
- #0981** 8:00am - 8:15am
DOES SLEEP DURATION INFLUENCE BODY MASS INDEX IN TWINS?
Watson N, Buchwald D, Vitiello M, Noonan C, Goldberg J
- #0979** 8:15am - 8:30am
INSOMNIA AND SLEEP DURATION AS MEDIATORS OF THE RELATIONSHIP BETWEEN DEPRESSION AND HYPERTENSION INCIDENCE IN MIDDLE-AGED SUBJECTS
Gangwisch J, Pickering T
- #0982** 8:30am - 8:45am
ADVERSE CARDIOMETABOLIC RISK AND NAPPING: THE GUANGZHOU BIOBANK COHORT STUDY
Arona T, Lam K, Jiang C, Zhang W, Cheng K, Thomas N, Lam T, Taheri S
- #0980** 8:45am - 9:00am
CONTRIBUTION OF FATIGUE TO CHEMOBRAIN IN WOMEN UNDERGOING CHEMOTHERAPY FOR BREAST CANCER
Ancoli-Israel S, Natanajan L, Palmer B, Parker B, Mills P, Sadler G, Dimsdale J
- #0984** 9:00am - 9:15am
SODIUM OXYBATE IMPROVES PAIN, FATIGUE, AND SLEEP IN FIBROMYALGIA: RESULTS FROM A 14-WEEK RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL
Swick T, Alvarez-Horine S, Zheng Y, Rothman J, Inhaber N, Holman A, Smith T, Russell I
- #0985** 9:15am - 9:30am
SLEEP-DISORDERED BREATHING (SDB) SYMPTOMS AND ASTHMA CONTROL IN THE ELDERLY
Teodorescu M, Polomis D, Peterson A, Consens F, Chervin R, Teodorescu M
- #0983** 9:30am - 9:45am
FREQUENT SNORING DURING PREGNANCY IS ASSOCIATED WITH AN INCREASED RISK OF GESTATIONAL DIABETES
Facco F, Grobman W, Lu B, Kramer J, Ho K, Zee P
- #0978** 9:45am - 10:00am
SLEEP DISORDERED BREATHING IN PATIENTS TAKING OPIOIDS FOR CHRONIC PAIN
Jungquist C, Yurcheschen M, Greenblatt D, Modrak J, Robert I, Grant B, Perlis M
- REFRESHMENT BREAK**
10:00am - 10:15am

SCIENTIFIC PROGRAM

Thursday, June 11, 2009

SYMPOSIA

10:15am – 12:15pm

S 25: Seizing the Event: The Sleeping Epileptic Child

10:15am – 12:15pm

Rooms 611-614

Chair: Sanjeev Kothare, MD, FAASM

Faculty: Matthew Anderson, MD, PhD; Oliviero Bruni, MD; Oscar Capdevila, MD

10:15am - 10:45am **The Close Relationship between the Bedfellows: Epilepsy and Sleep**
Matthew Anderson, MD, PhD

10:45am - 11:15am **The Undefined Boundaries between Epileptic and Non-epileptic Events during Sleep**
Oliviero Bruni, MD

11:15am - 11:45am **EEG Abnormalities in Sleep: Abnormal, Normal Variants and Artifacts**
Oscar Capdevila, MD

11:45am - 12:15pm **Polysomnographic Abnormalities in Children with Epilepsy**
Sanjeev Kothare, MD, FAASM

Objectives:

1. Describe the complex relationship between epilepsy and sleep.
2. Discuss the clinical semiology, interictal/ictal EEG patterns of the epilepsy syndromes in children which occur predominantly out of sleep.
3. Differentiate nocturnal seizures in children from other causes of sleep related arousals (“epilepsy mimics”).
4. Assess the polysomnographic abnormalities seen in children with epilepsy.

S 26: Neuropsychiatric Comorbidities of Obstructive Sleep Apnea Syndrome

10:15am – 12:15pm

Ballroom 6E

Chair: Hrayr Attarian, MD, FAASM

Faculty: Devin Brown, MD; Joel Dimsdale, MD; Paul Macey, PhD

10:15am - 10:45am **Neurocognitive Effects of OSA**
Hrayr Attarian, MD, FAASM

10:45am - 11:15am **CVA and OSA**
Devin Brown, MD

11:15am - 11:45am **Structural Brain Changes in Obstructive Sleep Apnea**

Paul Macey, PhD

11:45am - 12:15pm **Panel Discussion**

Faculty

Objectives:

1. Describe the impact of OSA on neurocognitive functions and the interplay between mood disturbances and OSA.
2. Discuss the relationship between cerebrovascular disease and OSA.
3. Review the different brain areas affected by OSA.

S 27: Brain Imaging of Insomnia: Hyperarousal, Hypoactivation or Compensatory Mechanisms?

10:15am – 12:15pm

Ballroom 6A

Chair: Ellemarije Altena

Faculty: Celyne Bastien, PhD; Sean Drummond, PhD; Dieter Riemann, MD, PhD

10:15am - 10:45am **Prefrontal Correlates of Insomnia as Shown by Structural and Functional Imaging Data in Older Adults**

Ellemarije Altena

10:45am - 11:15am **Chronic Insomnia: Hyperarousal and/or Inhibition Deficits? An ERPs Investigation**

Celyne Bastien, PhD

11:15am - 11:45am **Manual Morphometry Measures and Resting State fMRI in Chronic Insomnia**

Dieter Riemann, MD, PhD

11:45am - 12:15pm **Hypoactivation or Compensatory Mechanisms? Functional Neuroimaging Data of Insomnia in Younger Adults**

Sean Drummond, PhD

Objectives:

1. Review the neural mechanisms of chronic primary insomnia.
2. Explore the cause and possible consequences of the condition of insomnia.
3. Explain how the brain deals with insomnia.
4. Discuss whether the brain compensates for insomnia, resulting in mostly unaffected behavioral performance, yet with subjective complaints of difficulties with daytime function.
5. Discuss whether intact performance is the result of a combination of baseline hyperarousal and attenuated brain activation resulting from disturbed sleep.

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ORAL PRESENTATIONS

10:15am – 12:15pm

Authors selected for oral presentations are allotted a 10-minute time period to present their abstract, followed by a 5-minute time period for questions and answers. The four-digit abstract number corresponds to the abstract book.

22: Sleep and Memory Consolidation

10:15am – 12:15pm

Ballroom 6B

Chair: Sara Mednick, PhD

Objective: Detect the relationship between sleep variables and cognition.

- #1241 10:15am - 10:30am
SLEEP DEPRIVATION AFFECTS MULTIPLE DISTINCT COMPONENTS OF COGNITIVE PROCESSING
Van Dongen H, Childers R, Belenky G, Ratcliff R
- #1237 10:30am - 10:45am
SLEEP-DEPENDENT EXTRACTION & CONSOLIDATION OF EPISODIC MEMORY DETAILS
van der Helm E, Gujar N, Nishida M, Watts C, Walker M
- #1244 10:45am - 11:00am
SLEEP PROMOTES LASTING CHANGES IN MEMORY FOR EMOTIONAL SCENES
Payne J, Kensinger E, Wamsley E, Stickgold R
- #1243 11:00am - 11:15am
THE DREAM REPETITION CONTINUUM AND ITS RELATIONSHIP TO WELL-BEING
Zadra A, Miller M, Donderi D
- #1238 11:15am - 11:30am
BOLD ACTIVITY ENHANCEMENT DURING nREM SLEEP FOR CONSOLIDATION OF PERCEPTUAL LEARNING
Sasaki Y, Yotsumoto Y, Watanabe T
- #1240 11:30am - 11:45am
SLEEP SELECTIVELY ENHANCES HIPPOCAMPUS-DEPENDENT MEMORY IN MICE
Cai D, Shuman T, Gorman M, Sage J, Anagnostaras S
- #1239 11:45am - 12:00pm
DIFFERENTIAL DISRUPTION OF EXECUTIVE FUNCTION, ON WAKING FROM MORNING AND AFTERNOON NAPS, IN SLEEP RESTRICTED SUBJECTS
Groeger J, Lo J, Dijk D

- #1242 12:00pm - 12:15pm
SDB AND COGNITIVE FUNCTIONS IN THE TUCSON CHILDREN'S ASSESSMENT OF SLEEP APNEA (TUCASA) STUDY; 5 YEARS AFTER INITIAL ASSESSMENT
Archbold K, Goodwin J, Quan S

23: Circadian Misalignment: Impact and Therapy

10:15am – 12:15pm

Ballroom 6C

Chair: Orfeu Buxton, PhD

Objective: Examine treatments for circadian rhythm sleep disorders and methods for altering normal circadian rhythms.

- #0132 10:15am - 10:30am
THE NON-24 HOUR PERIOD OF THE REST/ACTIVITY CYCLE IS IDENTICAL TO THAT OF THE FREE-RUNNING MELATONIN RHYTHM IN BLIND AND SIGHTED INDIVIDUALS
Emens J, Laurie A, Songer J, Lewy A
- #0139 10:30am - 10:45am
CIRCADIAN RHYTHMS, PHYSICAL ACTIVITY AND THEIR INFLUENCE ON SLEEP-WAKE REGULATION DURING AN ANTARCTIC SUMMER EXPEDITION
Pattyn N, De Valck E, Cortoos A, Pirrena S, Neyt X, Cluydts R
- #0134 10:45am - 11:00am
CIRCADIAN PHASE IN PATIENTS WITH SHIFT-WORK DISORDER (SWD): INFLUENCE ON NIGHTTIME SLEEPINESS, PERFORMANCE AND DAYTIME SLEEP
Wright K, Dinges D, Roth T, Walsh J, Czeisler C
- #0129 11:00am - 11:15am
A COMPROMISE CIRCADIAN PHASE POSITION FOR PERMANENT NIGHT WORK IMPROVES NIGHT SHIFT ALERTNESS AND IS COMPATIBLE WITH LATE NIGHTTIME SLEEP ON DAYS OFF
Smith M, Fogg L, Eastman C
- #0133 11:15am - 11:30am
THE EFFECT OF DIURNAL PREFERENCE ON SUBJECTIVE ALERTNESS AND PERFORMANCE DURING EXTENDED WAKEFULNESS
Chang A, Stephens J, Ukaegbu V, Silva E, Duffy J

SCIENTIFIC PROGRAM

Thursday, June 11, 2009

#0128 11:30am - 11:45am
A NEW 0.5 MG MELATONIN PHASE RESPONSE CURVE IN HUMANS

Burgess H, Revell V, Molina T, Eastman C

#0135 11:45am - 12:00pm
ATTENUATING NOCTURNAL LIGHT INDUCED DISRUPTION IN ENDOCRINE, GENETIC AND BEHAVIORAL CIRCADIAN RHYTHM PHASE MARKERS BY FILTERING SHORT WAVELENGTHS

Rahman S, Marcu S, Shapiro C, Brown T, Casper R

#0137 12:00pm - 12:15pm
THE MELANOPSYN-MEDIATED DIRECT EFFECTS OF LIGHT ON SLEEP AND THE EEG INTERACT WITH THE CIRCADIAN AND HOMEOSTATIC DRIVE

Tsai J, Hannibal J, Hagiwara G, Colas D, Ruppert E, Hubbard J, Stephenson K, Heller C, Franken P, Bourgin P

Late-breaking Abstracts

10:15am – 12:15pm

Rooms 606-609

Chair: Terri Weaver, PhD, RN

Authors selected for the late-breaking abstract session are allotted a 10-minute time period to present their abstract, followed by a 5-minute time period for questions and answers. The late-breaking abstracts presented during this session are on pages 145-149.

CME and CE for psychologists are not provided for this session

LBA 1 10:15am – 10:30am
ENERGY RESTORATIVE FUNCTION OF SLEEP: EVIDENCE FROM CHANGING LEVELS OF ATP AND THE ACTIVATION OF AMP-ACTIVATED PROTEIN KINASE IN RAT BRAIN

Dwonak M, Kim T, Nipa F, Kalinchuk A, McCarley R, Basheer R

LBA 2 10:30am – 10:45am
GENOME-WIDE ASSOCIATION ANALYSIS OF SLEEP LENGTH REVEALS NEW GENES AND PATHWAYS CONTROLLING SLEEP HOMEOSTASIS

Ollila H, Partonen T, Kronholm E, Männistö S, Lönnqvist J, Salomaa V, Palotie L, Perola M, Porkka-Heiskanen T, Paunio T

LBA 3 10:45am – 11:00am
COMPETING PRESSURE FOR REM SLEEP PREVENTS HOMEOSTATIC RESPONSE OF SLOW-WAVE SLEEP DURING REPEATED PARTIAL SLEEP RESTRICTION

Chapoutot F, Leproult R, Tasali E, Nedelcheva A, Spiegel K, Van Cauter E

LBA 4 11:00am – 11:15am
PURINE TYPE 2-X7 RECEPTOR (P2X7R) KNOCKOUT MICE HAVE ATTENUATED SLEEP RESPONSES TO SLEEP LOSS AND LPS

Winters B, Szentirmai E, Krueger J

LBA 5 11:15am – 11:30am
POOR SUBJECTIVE SLEEP QUALITY IS ASSOCIATED WITH A DECREASED VOLUME OF THE CA3/DENTATE GYRUS HIPPOCAMPAL SUBFIELD

Neylan T, Wang Z, Mueller S, Marmar C, Weiner M, Schuff N

LBA 6 11:30am – 11:45am
DREAMING OF A LEARNING TASK IS ASSOCIATED WITH ENHANCED SLEEP-DEPENDENT MEMORY CONSOLIDATION

Wamsley E, Tucker M, Payne J, Benavides J, Stickgold R

LBA 7 11:45am – 12:00pm
NIGHTLY TREATMENT OF PRIMARY INSOMNIA WITH PROLONGED RELEASE MELATONIN FOR 6 MONTHS: AGE AND ENDOGENOUS MELATONIN AS PREDICTORS OF EFFICACY AND SAFETY

Wade A, Ford I, Crawford G, McMahon A, Nir T, Laudon M, Zisapel N

LBA 8 12:00pm – 12:15pm
EFFICACY OF CPAP TREATMENT IN MILDER SLEEPY OSA PATIENTS: RESULTS OF THE CATNAP RANDOMIZED CLINICAL TRIAL

Weaver T, Kuna S, Maislin G, Mancini C, Ferguson K, Schulman D, Greenberg H, Rapoport D, Chiong T and the CATNAP Study Group

THURSDAY

SCIENTIFIC PROGRAM

Thursday, June 11, 2009

Late-breaking Abstracts

10:15am – 12:15pm

Rooms 606-609

Chair: Terri Weaver, PhD, RN

LBA 1 10:15am – 10:30am

ENERGY RESTORATIVE FUNCTION OF SLEEP: EVIDENCE FROM CHANGING LEVELS OF ATP AND THE ACTIVATION OF AMP-ACTIVATED PROTEIN KINASE IN RAT BRAIN

Dworak M, Kim T, Nipa F, Kalinchuk A, McCarley R, Basbeer R
Psychiatry, Boston VA Healthcare System and Harvard Medical School, West Roxbury, MA, USA

Introduction: Sleep has been hypothesized to restore energy depleted during wakefulness, but there is little experimental support. Consequently, we examined sleep-wake changes in brain adenosine triphosphate (ATP), the universal energy currency in cells. We hypothesized that changes in ATP levels would be associated with changes in the phosphorylation state of AMP-activated protein kinase (P-AMPK), which is both a primary sensor of cellular energy and responsible for maintaining the balance between anabolic and catabolic pathways. High energy consuming states increase P-AMPK, while low energy consuming states decrease P-AMPK. We thus hypothesized that wakefulness and sleep deprivation (SD) would be associated with low ATP/high P-AMPK while high ATP/low P-AMPK would be seen in recovery sleep (RS) and spontaneous sleep.

Methods: Frontal cortex (FC), basal forebrain (BF), cingulate cortex (CCX) and hippocampus (HIP) samples from male Sprague-Dawley rats (12-hr light-dark cycle) were collected every 3h from lights on at 7 am up to 12h later, after 3h or 6h SD; and after RS. Bioluminescence detection measured ATP. Western-blot analysis measured phosphorylation of AMPK.

Results: After 3h of spontaneous sleep (10AM) ATP concentrations show a significant increase relative to 7AM in all tested brain regions, followed by a gradual decrease at 1, 4 and 7PM (ANOVA, $p < 0.001$). SD for 3h (beginning at 7AM) prevented this increase and 6h SD significantly decreased ATP. Following 3h SD, BF ATP increased after 3h RS, and in other regions after 6h RS. After 6h SD, ATP increased in all regions after 3h of RS. In BF, P-AMPK levels showed significant decreases after 3h of spontaneous sleep as well as RS and increases after 3h of SD, a reciprocal relationship to ATP levels.

Conclusion: These data support our hypotheses and provide molecular evidence for the energy restorative function of sleep and for P-AMPK as a key sensor of energy need.

Support: This work was supported by VA Medical Research Award and MH039683.

LBA 2 10:30am – 10:45am

GENOME-WIDE ASSOCIATION ANALYSIS OF SLEEP LENGTH REVEALS NEW GENES AND PATHWAYS CONTROLLING SLEEP HOMEOSTASIS

Ollila H^{1,2,3}, Partonen T¹, Kronholm E¹, Männistö S¹, Lönnqvist J¹, Salomaa V¹, Palotie L⁴, Perola M¹, Porkka-Heiskanen T², Paunio T^{1,3}

¹National Institute for Health and Welfare

²Department of Physiology, Institute of Biomedicine, University of Helsinki, Helsinki, Finland

³Department of Psychiatry, University of Helsinki and Helsinki University Central Hospital, Helsinki, Finland

⁴Welcome Trust Sanger Institute, Cambridge, UK

Introduction: The genetic component in sleep homeostatic and circadian regulation is high. Disturbances in sleep have also been linked to mood disorders like major depression or bipolar disorder. Furthermore, especially short sleep predisposes to metabolic syndrome and may induce weight gain. However, the molecular mechanisms behind sleep homeostasis are not yet well understood. Our aim was to further elucidate the genetic component in sleep regulation.

Methods: In order to further explain the variation in sleep length and seasonal rhythms we performed a genome-wide DNA association analysis of 2200 Finnish individuals from the national Health 2000 project. The individuals were genotyped with altogether over 600 000 single nucleotide polymorphism (SNPs) by Illumina 610K and characterized for sleep length per night (total sleep length or TLS) as well as evaluated for depressive symptoms and variation in mood due to seasonal changes. In addition to straight-forward search for association of the single polymorphisms, we also examined if there were enriched associations of variants from genes from distinct molecular pathways in our dataset.

Results: We found several new genes and variants that showed statistically significant association to total sleep length. Interestingly, the gene ontology analysis showed that sleep length and seasonal changes in mood share common molecular genes and pathways.

Conclusion: Altogether we have identified new genes for sleep homeostasis and found potential candidate genes for studying the pathological aspects of both sleep disturbances and mood disorders. Our findings also further support the idea that sleep disturbances and mood disorders may share common genetic components.

SCIENTIFIC PROGRAM

Thursday, June 11, 2009

LBA 3 10:45am – 11:00am

COMPETING PRESSURE FOR REM SLEEP PREVENTS HOMEOSTATIC RESPONSE OF SLOW-WAVE SLEEP DURING REPEATED PARTIAL SLEEP RESTRICTION

Chapotot F¹, Leproult R¹, Tasali E¹, Nedelcheva A¹, Spiegel K², Van Cauter E¹

¹Sleep, Neuroendocrinology and Chronobiology Research Laboratory, Department of Medicine, The University of Chicago, USA

²INSERM U628, Department of Experimental Medicine, University Claude Bernard, Lyon, France

Introduction: Chronic partial sleep restriction (PSR) is highly prevalent in modern societies. While most studies have documented a rapid eye-movement (REM) sleep deficit under such conditions, it remains unclear whether the homeostatic control of slow-wave sleep (SWS) is preserved. This study examines the dynamics of SWS and REM sleep regulation during repeated PSR and after recovery.

Methods: Fifteen healthy lean adults (14 men; 23±3 years) were studied in the laboratory during 16 consecutive nights with bedtimes of 8-h in the first 3 baseline nights (B1-B3), 4-h in the next 6 restriction nights (R1-R6), and 12-h in the last 7 extension nights (E1-E7). Center of the bedtime period was maintained constant to avoid shifts of circadian phase. Sleep was polysomnographically recorded and visually analyzed. Quantitative EEG and EOG automatic REM detection for the definition of phasic REM sleep (PREMS) were performed on nights B2, R5, and E1, while no blood sampling was performed. Parametric statistical analyses used log-transformed data using ANOVA and Bonferroni's multiple comparisons.

Results: Circadian phase stability was confirmed from melatonin and body temperature profiles. SWS remained unaffected and did not rebound after recovery. Overall sleep slow-wave activity (SWA - EEG power in the 0.75-4.5 Hz band) did not vary significantly. Despite significantly increased time points in the beginning of the first sleep cycle in R5 and E1, maximal SWA levels were not increased and occurred in the first instead of the second half-cycle at baseline. In contrast, REM sleep decreased in R5 ($p<0.05$) and increased in E1 ($p<0.05$) relative to B2. During the first 4 bedtime hours, REM sleep increased from B2 to R5 (ns) and E1 ($p<0.05$). PREMS decreased in R5 and rebounded significantly in E1, mostly in the first cycle. Linear regression analysis demonstrated a robust negative correlation between SWA and PREMS ($r = -0.456$, $p<0.001$).

Conclusion: Despite cumulative sleep debt, SWS did not show clear compensatory responses, contrasting with a massive rebound in REM sleep. The negative association between SWA and PREMS reveals the competing pressure for SWS and REM sleep, which may well lead to a state of allostasis during repeated PSR.

Support: This work was supported by grants PO1 AG-11412, RO1 HL-72694, RO1-75025, UL1 RR024999 and DK-20595 from the National Institute of Health, and Contract W81XWH-07-2-0071 from the Department of Defense PRMRP.

LBA 4 11:00am – 11:15am

PURINE TYPE 2-X7 RECEPTOR (P2X7R) KNOCKOUT MICE HAVE ATTENUATED SLEEP RESPONSES TO SLEEP LOSS AND LPS

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Introduction: The property of wakefulness that induces production of sleep regulatory substances (SRSs) remains unknown. Previously we proposed that ATP, co-released during neuro- and glia-transmission acting on P2Rs leads to the release of SRSs. The P2X7R is involved in glia release of interleukin-1 and tumor necrosis factor; two well characterized SRSs. In P2X7R-knockout (KO) mice, release of IL-1 β from microglia in response to lypopolysaccharide (LPS) and ATP is reduced. ATP agonists promote, while ATP antagonists inhibit, sleep in rats. Further, somatosensory cortical levels of P2X7R vary with sleep propensity. We thus posited that mice lacking the P2X7R would have altered sleep responses to sleep loss and microbial challenge.

Methods: Wild type C57BL6 mice (WT) and P2X7KO mice, (Jackson Laboratory, n=5 each group) were on a 12:12 h light-dark cycle and provided with EEG and EMG electrodes for sleep and EEG power analyses. After baseline recordings animals were sleep deprived for 6 h prior to dark onset. In a separate experiment, 1 μ g of LPS in 0.1 ml saline was injected intraperitoneally at dark onset and sleep was recorded for 24 h.

Results: Increase in the duration of sleep during the first 6 h after sleep deprivation in the P2X7KO mice were 54% for nREM and 41% for REM of that observed in WT mice. Increase in EEG delta power during nREM was 12% of that observed in WT mice during the same period. P2X7KO mice, unlike WT mice, failed to increase nREM sleep in the first 4 h after LPS injection. Further, nREM sleep delta power was reduced in WT, but not in the P2X7KO mice after LPS challenge.

Conclusion: Results suggest that P2X7Rs are involved in sleep regulation and support the hypothesis that ATP signaling is used to keep track of wakefulness. Results also clearly demonstrate independent regulation of sleep state duration and EEG power.

Support: NIH grants NS25378 and NS31453

THURSDAY

SCIENTIFIC PROGRAM

Thursday, June 11, 2009

LBA 5 11:15am – 11:30am

POOR SUBJECTIVE SLEEP QUALITY IS ASSOCIATED WITH A DECREASED VOLUME OF THE CA3/DENTATE GYRUS HIPPOCAMPAL SUBFIELD

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Introduction: An emerging literature has shown that prolonged disruption of sleep impairs neurogenesis in animals particularly in the CA3/dentate gyrus hippocampal subfields. We developed a reliable measure of hippocampal subfields in humans using high field strength MRI. Our initial objective was to determine if Posttraumatic Stress Disorder (PTSD) was associated with structural alterations in the subfields of the hippocampus. Our second objective was to specifically examine the relationship of sleep quality to the CA3/dentate subfield.

Methods: Volumes of hippocampal subfields in seventeen veteran males positive for PTSD (41 ±12 years) and nineteen age-matched male veterans negative for PTSD were measured using 4 Tesla MRI. Subjective sleep quality was measured by the Pittsburgh Sleep Quality Index (PSQI) and the Insomnia Severity Index (ISI).

Results: PTSD was associated with 11.3 ± 1.5% (p = 0.006) smaller CA3/dentate subfield volumes, whereas other subfields were spared. There was considerable overlap in sleep quality in the two groups: 5 PTSD subjects had better sleep quality than the comparison group. There was a strong inverse correlation between the mean volumes of the CA3/dentate subfields and the PSQI score (r = -.52, p = 0.001) in the combined sample. Adding the PSQI score to a hierarchical linear regression model after first accounting for age and PTSD symptoms produced a 13 % increase in incremental variance (t = -2.44, p = 0.02). Despite the high correlation between PTSD symptoms and the PSQI score, subjective sleep quality was the best predictor of the CA3/dentate volume and accounted for unique variance beyond PTSD. The ISI produced nearly identical results.

Conclusion: The findings indicate for the first time in humans that poor sleep quality is associated with volume loss of the CA3/dentate subfields. This is consistent with animal studies showing that chronic sleep disruption is associated with decreased neurogenesis and dendritic branching in these structures.

Support: This research was supported in part by grants from the Mental Illness Research and Education Clinical Center (MIRECC) of the US Veterans Health Administration, Office of Research and Development, the Department of Defense, and the National Center for Research Resource of NIH (RR23953). This material is the result of work supported with resources and the use of facilities at the Veterans Administration Medical Center, San Francisco, California.

LBA 6 11:30am – 11:45am

DREAMING OF A LEARNING TASK IS ASSOCIATED WITH ENHANCED SLEEP-DEPENDENT MEMORY CONSOLIDATION

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Introduction: It is now well established that post-learning sleep is beneficial for human memory. This mnemonic benefit is thought to be associated with the neural-level reactivation and re-organization of memory traces in the sleeping brain. In the present study, we explored whether sleep-dependent memory processing might be directly observable within the content of human dream experiences.

Methods: Participants (n=99) were trained at 12:30pm on a 3D-style virtual maze task, previously shown to be sleep-dependent. Subjects then either lay down for a 1.5 hr nap opportunity (n=50), or remained awake (n=49). During this period, all subjects were prompted to make open-ended verbal reports of “everything that was going through your mind”. Additionally, a questionnaire directly probed a subset of participants (n=47) as to whether they had experienced task-related mentation during the retention interval. Subjects were retested on the maze at 5:30pm.

Results: Task-related mentation was strongly associated with enhanced performance at retest, whether measured by questionnaire or open-ended verbal report. Sleep participants who reported maze-related mentation on the questionnaire (n=12) improved significantly more across the retention interval than did Sleep participants without maze-related mentation (t₂₀=4.02, p<.001). In contrast, thinking of the maze while awake did not provide any performance benefit (p>.8; condition x mentation interaction: p=.006). In the Sleep group, the four participants (8.0%) who spontaneously referenced the maze in their open-ended reports improved tenfold more at retest than Sleep participants (n=46) without task-related reports (t₄₈=3.88, p=.0003). Again, thinking of the maze while awake (n=2) was not associated with improvements in completion time (condition x mentation interaction: p=.08).

Conclusion: These data comprise novel evidence that dream mentation reflects the learning-induced reactivation of memory networks during sleep, and is correlated with substantial enhancement of memory performance.

Support: This research was supported by grants R01-MH48832, R01-65292 and T32-HL07901 from the NIH.

SCIENTIFIC PROGRAM

Thursday, June 11, 2009

LBA 7 11:45am – 12:00pm

NIGHTLY TREATMENT OF PRIMARY INSOMNIA WITH PROLONGED RELEASE MELATONIN FOR 6 MONTHS: AGE AND ENDOGENOUS MELATONIN AS PREDICTORS OF EFFICACY AND SAFETY

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Introduction: Melatonin is extensively used for circadian rhythm and other sleep disorders. However, well controlled studies of such use and particularly of long term efficacy and safety are lacking. Prolonged release melatonin (PRM; Circadin® 2 mg, Neurim Pharmaceuticals) is approved in the EU for treatment of insomnia in patients aged >55. Because melatonin production declines with age it was pertinent to ask whether PRM efficacy is related to patient's endogenous melatonin (6-sulfatoxymelatonin [6SMT] ≤8 or >8 µg/night) or age (≥65 or <65) and sustained over long term periods.

Methods: 791 adult outpatients (age 18-80 years) with primary insomnia were treated with placebo (2 weeks) and randomized, double-blind, to 3 weeks with PRM or placebo nightly. Completers were randomized to PRM or placebo for 26 weeks. Sleep was recorded daily (Diary). Pittsburgh Sleep Quality Index (PSQI), Quality of life (WHO-5) Clinical Global Impression of Improvement (CGI-I) adverse effects and vital signs were recorded at each visit. Rebound insomnia and withdrawal effects were evaluated during 2 weeks placebo run-out.

Results: No evidence was found that PRM affects sleep latency or quality in 6SMT low excretors aged 18-80 years. In patients aged >65 PRM (3 weeks) significantly reduced sleep latency (-19.1 vs. -1.7 minutes p=0.002) and improved global PSQI (p=0.042) compared with placebo. Over the 6 months extension, PRM efficacy was maintained demonstrating reduced sleep Latency (p<0.001) and improved global PSQI (p=0.003) compared to placebo. No withdrawal symptoms or rebound insomnia were detected after PRM discontinuation. Most adverse events were mild in severity with no apparent differences between treatment groups in any safety outcome.

Conclusion: This is the first study demonstrating long term efficacy and safety of PRM in insomnia patients. Age rather than 6SMT excretion predicts response to PRM therapy.

Support: ClinicalTrials.gov ID: NCT00397189

LBA 8 12:00pm – 12:15pm

EFFICACY OF CPAP TREATMENT IN MILD SLEEPY OSA PATIENTS: RESULTS OF THE CATNAP RANDOMIZED CLINICAL TRIAL

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Introduction: There is limited evidence regarding whether CPAP positively affects functional status in patients with mild to moderate OSA. Results from randomized controlled studies examining this issue have produced conflicting results principally because of serious methodological limitations. Therefore, it remains unclear whether CPAP treatment improves daily functioning in those with milder disease. We conducted a clinical trial to test the hypothesis that the mean increase (improvement) in the Functional Outcomes of Sleep Questionnaire (FOSQ) Total score, would be larger for active CPAP compared to sham CPAP after 8 weeks of treatment in sleepy patients with milder OSA.

Methods: We conducted a 5 site, international, double blind, randomized, placebo-controlled parallel groups study of the functional improvement efficacy of CPAP treatment in sleepy (ESS > 11) patients with mild to moderate OSA (AHI 5 – 30). Patients were randomized to 8 weeks of either active CPAP or sham treatment followed by 8 weeks cross-over of sham group to open label active treatment.

Results: Of the 281 patients who were randomized, 239 were randomized and exposed (N=121 active and N=118 sham). Randomized unexposed patients (N=42) were excluded from all analyses. Mean ages were 49.5 and 51.7 yrs, respectively, with 55% and 63% males, respectively. Total sample size was 223 (113 Active, 110 Sham) for primary Intent To Treat analyses. The mean changes from baseline to Week 8 were 0.98 (SD=2.89, N=113) and -0.14 (2.61, N=110), (Effect Size = 0.41) active and sham cohorts, respectively. Based on the ANCOVA model, the adjusted group difference in mean changes from pre treatment baseline to Week 8 was 0.95 points (95% CI 0.27 to 1.62; p=0.006).

Conclusion: This randomized clinical trial demonstrated a clinically relevant and statistically significant improvement in functional status at 8 weeks on active CPAP therapy compared to sham CPAP therapy.

Support: Grant support from the National Heart, Lung, Blood Institute, Respiroics Respiratory, Sleep Research Foundation and the American Academy of Sleep Medicine.

THURSDAY