

INVITED SPEAKERS

Alex Iranzo

Neurology Service, Hospital clinic de Barcelona, Spain.

<http://www.thelancet.com/journals/laneur/article/PIIS1474-4422%2807%2970121-7/fulltext>

Title: REM sleep behaviour disorder as a specific marker of Parkinson disease.

REM sleep behaviour disorder (RBD) is a parasomnia characterized by dream-enacting behaviours linked to nightmares and REM sleep without atonia. RBD can be classified into an idiopathic form and into a secondary form associated with the synucleinopathies, focal brainstem lesions, the use of antidepressants and narcolepsy. It has been shown that about 90% patients with the idiopathic form of idiopathic RBD eventually develop Parkinson disease and other synucleinopathies if they are followed-up during a 14 year period. Those patients who remain idiopathic usually show markers of PD such as mild cognitive impairment, reduced dopamine transporter imaging in the putamen, hyperechogenicity of the substantia nigra and hyposmia. Idiopathic RBD provides an optimal target to study PD disease onset and progression during its prodromal stage and to test disease-modifying interventions to slow down or stop the degenerative process before parkinsonism is evident.

Biosketch Alex Iranzo

Alex Iranzo graduated Medicine (1991) and Neurology (1997) and defended his PhD thesis (2002) entitled "Sleep disorders in the parkinsonian syndrome" at the Universidad de Barcelona, Spain. Presently, he is neurologist consultant at the Neurology Service and at the Multidisciplinary Sleep Unit of the Hospital Clinic of Barcelona, Barcelona, Spain. He is investigator of Institute D' Investigacions Biomèdiques August Pi i Sunyer and CIBERNED. He is a member of numerous national and international Neurology, Sleep, REM sleep behavior disorder and Restless Legs societies and is currently secretary of the International REM sleep behaviour disorder group, treasurer of the Sleep Spanish Society, and assistant treasurer of the World Association of Sleep Medicine. Dr. Iranzo has widely published as both first and corresponding author in peer reviewed journals such as The Lancet, The Lancet Neurology, Annals of Neurology, Neurology, Journal of Neurology Neurosurgery and Psychiatry, Movement Disorders, Sleep, and Sleep Medicine. Dr. Iranzo research has focused in sleep in neurological diseases including Parkinson's disease, REM sleep behaviour disorder, narcolepsy and restless legs syndrome.

Marcos Frank

University of Pennsylvania, School of Medicine, Philadelphia, USA

<http://www.med.upenn.edu/apps/faculty/index.php/g362/p36825>

Title: Sleep to weaken, sleep to strengthen: An integrative view of sleep and synaptic plasticity.

Biosketch Marcos Frank

Marcos Frank received his PhD in Neuroscience at Stanford University in 1997, where he worked in the laboratory of H. Craig Heller studying the ontogenesis of sleep and sleep regulation in rodents. This line of research provided new insights into sleep homeostasis in infancy and how this and related processes are altered by fetal exposure to psychoactive compounds. He then conducted post-doctoral research in the laboratory of Michael P. Stryker at the University of California, San Francisco demonstrating a role for sleep in a canonical form of *in vivo* cortical synaptic plasticity, originally described by David Hubel and Torsten Wiesel. He has continued this line of research as an Associate Professor at the University of Pennsylvania since 2003. Among other discoveries, the Frank lab has shown that sleep is associated with the activation of glutamate receptors and enzymatic pathways that consolidate experience-dependent plasticity in the cortex. A second line of research is focused on the role of glial astrocytes in sleep regulation. In collaboration with Dr.'s Phil Haydon and Ted Abel, Dr. Frank and his colleagues showed that astrocytic gliotransmission (*i.e.* the release of neurotransmitters by astrocytes) plays an important role in sleep homeostasis. Both research topics are active areas of investigation in the Frank laboratory, and work along these lines has appeared in the Journals *Neuron*, *Current Biology*, *Proceedings of the National Academy of Sciences*, *Journal of Neuroscience* and *SLEEP*. Dr. Frank is also the author of several review articles and book chapters on the topics of glial regulation of sleep, sleep function and the role of sleep in brain plasticity, and is the senior editor of *Current Advances in Sleep Biology* (Nova Biomedical Books, 2009) and *Brain Activity in Sleep* (Elsevier, 2012).

Yuval Nir

Sagol School of Neuroscience & Department of Physiology and Pharmacology, School of Medicine, Tel Aviv University

http://neuroscience-web.tau.ac.il/en/?post_type=portfolio&p=1301

Title Local brain oscillations of sleep and sleepiness: insights from intracranial EEG and single-unit recordings in humans

Slow waves and spindles, the hallmark brain oscillations of NREM sleep, have been mostly studied *in vitro*, under anesthesia, within few brain regions or with scalp EEG. We examined intracranial depth EEG and single-unit activity recorded simultaneously in up to 12 brain regions in neurosurgical epilepsy patients to better characterize regional diversity in sleep oscillations. We found changes in spindle occurrence, frequency, and timing between regions and across sleep, reflecting anatomical projections and changes in sleep depth. We further show that both slow waves (and the underlying active and silent neuronal states) and sleep spindles occur mostly locally, thereby showing that sleep involves constrained intracerebral communication. Slow waves also propagate, usually from medial prefrontal cortex to the medial temporal lobe and hippocampus.

A second line of research focuses on the effects of sleep deprivation. Recently, we showed that in rats, prolonged wakefulness leads to regional neuronal inactivity, low-frequency (2-6 Hz) waves, and behavioral

deficits. We have now also studied the neural correlates of sleepiness in awake, sleep deprived patients who performed face/place categorization in a modified Psychomotor Vigilance Task (PVT). Multiple sessions, some of which were conducted after full-night sleep deprivation, established that sleepiness leads to frequent behavioral lapses. During such lapses, visually-responsive neurons exhibited a reduced response 200-300ms after image onset, accompanied by a local increase in low-frequency LFP. These findings suggest that in humans, as in rats, “local sleep” during wakefulness may underlie the cognitive effects of sleepiness.

A final study compared neuronal activity associated with rapid eye movements during wakefulness and REM sleep. Immediately before REM onset, at times when behavioral saccadic suppression occurs, a reduction in firing was observed in neurons across multiple cortical and MTL regions, accompanied by distinct ERPs in intracranial EEG - akin to PGO potentials. This was followed by increased spiking activity peaking 300-400ms after REM onsets, with regional variability of exact timing that supports cortical-hippocampal propagation. The results suggest shared patterns of cortical neuronal activity associated with rapid eye movements during wakefulness and sleep in humans.

Biosketch Yuval Nir

Yuval Nir is an assistant professor at Tel-Aviv University, Israel. His lab studies sleep and its relation to cognition and consciousness in both humans and animals: <http://medicine.mytau.org/nir/>. Dr. Nir studied computer science, proceeded to a PhD in neurobiology (with Prof. Rafael Malach at the Weizmann Institute of Science, Israel) and completed a postdoctoral fellowship with Prof. Giulio Tononi at Madison, WI. Throughout his career, Dr. Nir has closely collaborated with Prof. Itzhak Fried in studying sleep and spontaneous activity in neurosurgical epilepsy patients, and has made a number of recent findings regarding local oscillations of sleep and sleepiness in the human brain.

Derk-Jan Dijk

Department of Biochemistry and Physiology, University of Surrey, Guilford

http://www.surrey.ac.uk/biochemistry/People/dijk_dj/

Title: Interaction between sleep and the human circadian system: from genes to cognition

Sleep and circadian rhythms are often investigated in separate experiments and settings but when they are studied simultaneously intimate two-way interactions become apparent. On the one hand sleep structure, sleep timing and sleep quality all depend on circadian phase. On the other hand the phase and amplitude of many circadian rhythms are affected by sleep-wake history. Thus the timing of the rhythm of melatonin is affected by sleep restriction and the amplitude of cognitive performance is markedly affected by sleep debt. Recently it has become apparent that these interactions are not limited to physiology and behaviour, but extend into the molecular components of circadian rhythmicity, including core clock genes. These data highlight the impact of sleep on many aspects of the temporal organization in humans and have implications for understanding the mechanisms underlying the negative health outcomes related to insufficient sleep.

Key References

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Biosketch Derk-Jan Dijk

Derk-Jan Dijk PhD, FSB, is Professor of Sleep and Physiology and Director of the Surrey Sleep Research Centre and Director of Sleep Wake Research of the Surrey Clinical Research Centre in the Faculty of Health and Medical Sciences at the University of Surrey, Guildford, UK. He is a Royal Society-Wolfson Research Award holder. He previously was a Senior Research Associate in the Institute of Pharmacology at the University of Zurich, an Assistant Professor of Medicine at Harvard Medical School, and an Associate Neuroscientist in the Brigham and Women's Hospital in Boston.

Dr Dijk has more than 25 years of experience in clinical sleep research. His current research interests include the pharmacological manipulation of sleep and cognition; the role of circadian rhythmicity in sleep regulation; identification of novel-biomarkers for susceptibility to the negative effects of sleep loss; understanding age and sex related differences in sleep physiology and sleep disorders. His research is funded by the Biotechnology and Biological Science Research Council, the Wellcome Trust, The Air Force Office of Scientific Research, Philips Lighting and several major pharmaceutical companies.

Dr Dijk has published more than 160 research and review papers in the area of sleep and circadian rhythms. Dr Dijk is invited frequently to speak at international sleep meetings and he has given opening and plenary lectures for the joint meeting of the Canadian Sleep Society, American Academy of Sleep Medicine and Sleep Research Society, The European Sleep Research Society and the Hong Kong Sleep Medicine Society.

Dr Dijk has served as an Associate and Deputy Editor to SLEEP and is currently Editor of the Journal of Sleep Research. He also serves as consultant to the pharmaceutical industry. Dr Dijk is vice-president of the World Sleep Federation.