Agenda
Parasomnias Section Meeting
Monday, June 13, 2011 5:15PM – 7:15PM
Minneapolis Convention Center – Room 205C

I. Welcome and Introduction – Dr. Milena Pavlova, Chair 5:15PM

II. Parasomnias Year-In-Review
   • Rafaeille Ferri, MD
     Improved Computation of the Atonia Index in Normal Controls and Patients with REM Sleep Behavior Disorder 5:20PM
   • Geert Mayer, MD
     Diffusion Tensor Imaging in Idiopathic REM Sleep Behavior Disorder Reveals Microstructural Changes in the Brainstem, Substantia Nigra, Olfactory Region, and other Brain Regions 5:40PM
   • Joan Santamaria, MD
     Decreased Striatal Dopamine Transporter Uptake and Substantia Nigra Hyperechogenicity as Risk Markers of Synucleinopathy in Patients with Idiopathic Rapid-Eye-Movement Sleep Behavior Disorder: A Prospective Study 6:00PM

III. Year-In-Review Speaker Discussion Panel 6:20PM

IV. Parasomnias Steering Committee Current/Future Initiatives 6:30PM

V. Open Floor for Attendees

VI. RBD Multicenter Trial Update 6:45PM

VII. Other Business

VIII. Adjournment
     Decreased striatal dopamine transporter uptake and substantia nigra

There is now general consensus that neurodegenerative diseases like Parkinson disease (PD) have latent periods where neuropathological changes are developing in the nervous system but have not reached the threshold for clinical symptoms to emerge or diagnosis to be established.

Also, it appears plausible to assume that neuroprotective or disease-modifying therapies might have their greatest chance of success if given in these early preclinical disease periods. Thus, identifying individuals in the preclinical phase of a neurodegenerative condition such as PD is a clinical and research priority.

Investigations in such individuals would allow studying disease progression in very early disease stages and testing drugs with potential disease-modifying effects before motor and cognitive symptoms have emerged. Furthermore, close follow-up of these subjects would allow establishing a diagnosis of these conditions at a very early stage and to start then a treatment that might improve their health status.

REM sleep behaviour disorder (RBD) is characterized by dream-enacting behaviours linked to REM sleep without atonia. Subjects with idiopathic REM sleep behaviour disorder (IRBD) may develop neurodegenerative conditions associated with substantia nigra dysfunction such as PD. In the early stages of PD, $^{123}$I-FP-CIT SPECT detects striatal dopamine dysfunction resulting from nigral pathology whereas transcranial sonography (TCS) shows increased substantia nigra echogenic size, even before parkinsonism is clinically evident. We hypothesized that these neuroimaging findings typical of PD may also occur in a proportion of IRBD individuals, who might then be at increased risk for developing a neurological syndrome associated with substantia nigra impairment like PD. In our study, 43 IRBD subjects and matched controls underwent $^{123}$I-FP-CIT SPECT and TCS. Two years and a half after neuroimaging, we assessed how many IRBD subjects developed a neurodegenerative syndrome and compared their neuroimaging results with those from patients that remained disease-free.

We found that 40% of the patients had reduced FP-CIT striatal binding, and 36% had substantia nigra hyperechogenicity on TCS. Twenty-seven (63%) subjects had decreased striatal FP-CIT binding and/or substantia nigra hyperechogenicity. As seen in early PD, IRBD patients had decreased FP-CIT uptake which was more marked in the putamen than in the caudate nucleus, increased substantia nigra echogenicity, and no correlation between FP-CIT uptake and echogenicity. Two years and a half later, eight (19%) subjects, all with reduced FP-CIT uptake and/or substantia nigra hyperechogenicity, developed clinically defined PD (n=5), dementia with Lewy bodies (n=2) or multiple system atrophy (n=1). Patients with normal neuroimaging remained disease-free after the same follow-up period. Our study showed that in IRBD, $^{123}$I-FP-CIT SPECT and TCS reveal subclinical changes which are typically seen in early PD. Decreased striatal FP-CIT binding and substantia nigra hyperechogenicity may be useful markers to identify IRBD individuals at increased short-term risk for developing the synucleinopathies PD, dementia with Lewy bodies and multiple system atrophy.

Improved computation of the atonia index in normal controls and patients with REM sleep behavior disorder.
Presented by Rafaelle Ferri

Despite the crucial relevance of the increased chin EMG activity during REM sleep for the diagnosis of RBD, only few systematic attempts have been carried out in order to analyze quantitatively submentalis muscle EMG activity during sleep probably because of the use, for decades, of paper recordings in sleep research. Basically, only three papers have appeared in the literature from 1992 to 2006, which have attempted to quantify submentalis muscle EMG activity in RBD patients by means of a visual approach, with the aim of counting the amount of epochs without atonia (elevated background EMG activity) and the amount of mini-epochs (2- to 3-second long) containing phasic EMG activity. In these studies, beside their simple and apparently quantitative parameters, no solid mathematical and quantitative definitions, in terms of amplitude and duration, have been provided for the elements taken into account: atonia, phasic and tonic EMG activations.

In recent years, some algorithms have been proposed to quantify automatically the amplitude of the chin EMG during REM sleep, in order to provide a tool useful for the diagnosis of RBD. Based on one of these algorithms we have developed the REM sleep Atonia Index that can vary from 0, that means complete absence of EMG atonia, to 1 or stable EMG atonia in the epoch. This Index, together with other measurements connected with our algorithm, was not only able to show differences between normal controls and patients, but also between nosologically different groups of patients who might present a different type of REM sleep-related motor disturbance which is today called RBD in all cases. So far, this index has been applied to normal controls (young adults and elderly), idiopathic RBD patients, subjects with multiple system atrophy, narcoleptics, and patients with Parkinson’s disease, for a total exceeding 150 subjects. This makes our index the best quantitative tool proposed so far for the detection of the main PSG marker of RBD.

Diffusion tensor imaging in idiopathic REM sleep behavior disorder reveals microstructural changes in the brainstem, substantia nigra, olfactory region, and other brain regions.

Presented by Geert Mayer

Idiopathic REM sleep behaviour disorder (iRBD) is a risk marker for the development of Parkinson’s disease (PD) and other alpha-synucleinopathies. Its pathophysiology is caused by a dysfunction of brainstem nuclei that regulate REM sleep and motor behaviour in REM sleep. These brainstem regions are also affected in evolving PD, suggesting a pathophysiological link between iRBD and PD. Clinical signs in early PD and iRBD such as hyposmia, impaired colour discrimination and neuropsychological deficits are similar in both disorders.

Diffusion tensor imaging (DTI) is a MRI technique for visualization of tissue organization in respect to microstructural integrity. The aim of the study was to investigate whether DTI allows detection of microstructural brain abnormalities in patients with iRBD (n=12) when compared to age-matched healthy controls (n=12). Whole-head DTI scans (measuring fractional anisotropy (FA) as well as radial and axial diffusivity) were analysed using track-based spatial statistics.

Group comparisons displayed significant microstructural brain tissue changes in the pons, the right substantia nigra, the olfactory cortex, the fornix, the visual system and the left temporal lobe. These regions that are also affected in evolving PD, are
known to regulate physiologic REM sleep. The reported microstructural changes in the olfactory cortex, the visual system and the left temporal lobe might represent structural correlates of symptoms of iRBD patients such as hyposmia and neuropsychological deficits.

The study shows, that RBD related neuropathology can be detected in vivo with a MRI technology.