

6th MOVEMENT DISORDERS TEACHING COURSE

**31 March - 1 April 2017 | Hotel Alpin
Poiana Brasov | Romania**



Welcome Address

It is a great pleasure to invite you to the 6th Movement Disorders Teaching Course in Poiana Brasov. Our event is designed for medical doctors involved in treating movement disorders patients. Senior physicians, residents, as well as students may find this education of value.

The Organizing Committee wishes you to have fruitful idea exchanges, interesting and interactive discussions.

This comprehensive two days course will approach various topics in the field of movement disorders. Video sessions will exemplify the phenomenology and will highlight the key learning message. Interaction with the audience and debate are strongly encouraged. The speakers at this course were selected based on their scientific experience, outstanding clinical reputation and excellent teaching skills.

We very much hope you will find our program of great interest and warmly wish you to have an enjoyable time in Poiana Braşov.

Course Director
CRISTIAN FALUP-PECURARIU

Co Chair Scientific Committee
OVIDIU BĂJENARU

Co Chair Scientific Committee
DAFIN F. MUREŞANU



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Course Director:



CRISTIAN FALUP-PECURARIU

Faculty of Medicine, Transilvania University
Head of the Department of Neurology,
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Brasov, Romania

Co Chair Scientific Committee:



OVIDIU BĂJENARU

Honorary President of the Romanian Society of Neurology
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Director of the Department of Neurology, Neurosurgery and
Psychiatry
Chairman and Head of Dept. Neurology - University Emergency
Hospital Bucharest

Co Chair Scientific Committee:



DAFIN F. MUREȘANU

President of the Romanian Society of Neurology
Co-Chair EAN Scientific Panel Neurorehabilitation
Vice President European Federation of NeuroRehabilitation
Societies (EFNR)
Professor of Neurology, Chairman Department of Neurosciences
"Iuliu Hatieganu" University of Medicine and Pharmacy,
Cluj-Napoca, Romania
Chairman "RoNeuro" Institute for Neurological Research and
Diagnostic
President of the Society for the Study of Neuroprotection
and Neuroplasticity (SSNN)



Faculty

(in alphabetical order)

Angelo Antonini /Italy
Keyoumars Ashkan /UK
Ovidiu Băjenaru /Romania
Roberta Biundo /Italy
Vincenzo Bonifati /The Netherlands
Adolfo Bronstein /UK
K. Ray Chaudhuri /UK
Fiorella Contarino /The Netherlands
Cristian Falup-Pecurariu /Romania
Sharon Hassin-Baer /Israel
Peter Jenner /UK
Meike Kasten /Germany
Dafin F. Mureșanu /Romania
Per Odin /Sweden/Germany
Walter Paulus /Germany
Lacramioara Perju-Dumbrava /Romania
Marios Politis /UK
Matej Skorwanek /Slovakia
Fabrizio Stocchi /Italy
Claudia Trenkwaldner /Germany



Scientific Program

Scientific Program

DAY 1 – 31 MARCH 2017

MORNING SESSION

Session 1 Chairman:	Ovidiu Băjenaru (Romania), Claudia Trenkwalder (Germany), Peter Jenner (UK)
08:45 – 09:00	Introduction
09:00 – 09:30	The clinical profiles of Parkinson’s disease patients Ovidiu Băjenaru/Romania
09:30 – 10:00	Pathophysiology of restless legs and augmentation Walter Paulus/Germany
10:00 – 10:30	Surgical therapies for Parkinson’s disease Keyoumars Ashkan/UK
10:30 – 11:00	Rehabilitation in Parkinson’s disease Dafin F. Mureșanu/Romania
11:00 – 11:30	Coffee-break
Session 2 Chairman:	Dafin F. Mureșanu (Romania), Keyoumars Ashkan (UK), Per Odin (Sweden/Germany)
11:30 – 12:00	Issues in the dopamine agonists treatment in Parkinson’s disease Cristian Falup-Pecurariu/Romania
12:00 – 12:30	Sexual dysfunction in Parkinson’s disease Sharon Hassin-Baer/Israel
12:30 – 13:00	Non-dopaminergic approaches to treating Parkinson’s disease Peter Jenner/UK
13:00 – 14:00	Lunch

DAY 1 – 31 MARCH 2017

AFTERNOON SESSION

Session 3 Chairman:

Walter Paulus (Germany), Lacramioara Perju-Dumbrava (Romania),
Sharon Hassin-Baer (Israel)

14:00 – 14:30

Pump-based Therapies for Advanced Parkinson's disease
Per Odin/Germany/Sweden

14:30 – 15:00

RBD - symptomatology, assessment and implications for
Parkinson syndromes
Claudia Trenkwalder/Germany

15:00 – 15:30

Speech and voice impairment in Parkinson's disease
Lacramioara Perju-Dumbrava/Romania

15:30 – 16:00

Genetics of Parkinson's disease
Vincenzo Bonifati/The Netherlands

16:00 – 16:30

Coffee break

Session 4 Chairman:

Vincenzo Bonifati (The Netherlands)

16:30 – 17:30

Video session

- a. Phenomenology of movement disorders
- b. Complex movement disorders - hypokinetic

20.00

Dinner

Scientific Program

DAY 2 – 1 APRIL 2017

MORNING SESSION

Session 5 Chairman:

K. Ray Chaudhuri (UK), Meike Kasten (Germany),
Adolfo Bronstein (UK)

09:00 – 09:30

Diagnostic approach to patients with dystonia
Matej Skorwanek/Slovakia

09:30 – 10:00

Eye movement abnormalities in patients with movement disorders
Adolfo Bronstein/UK

10:00 – 10:30

Non-motor symptoms –
clinical approach and therapeutic management
K. Ray Chaudhuri/UK

10:30 – 11:00

Neuroimaging in movement disorders
Marios Politis/UK

11:00 – 11:30

Coffee-break

Session 6 Chairman:

Marios Politis (UK), Cristian Falup-Pecurariu (Romania)

11:30 – 12:00

Gastrointestinal dysfunction in Parkinson's disease
K. Ray Chaudhuri/UK

12:00 – 12:30

The importance of an effective treatment: practical consideration
Fabrizio Stocchi/Italy

12:30 – 13:30

Lunch

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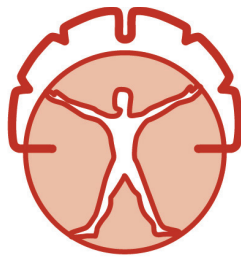
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DAY 2 – 1 APRIL 2017

AFTERNOON SESSION

Session 7 Chairman:	Angelo Antonini (Italy), Fabrizio Stocchi (Italy), Matej Skorwanek (Slovakia)
13:30 - 14:00	Cognitive decline in Parkinson's diseases: the complex picture Roberta Biundo/Italy
14:00 – 14:30	Treatment recommendations for motor symptom control in advanced Parkinson's diseases Angelo Antonini/Italy
14:30 – 15:00	Dystonia treatment Fiorella Contarino/The Netherlands
15:00 - 15:30	Epidemiology of Parkinson's disease Meike Kasten/Germany
15:30 - 16:00	Coffee break
Session 8 Chairman:	Fiorella Contarino (The Netherlands)
16:00 – 17:00	Video session Complex movement disorders - hyperkinetic
17:00 - 17:30	Closing remarks
20.00	Dinner

Endorsed by



International Parkinson and
Movement Disorder Society



Abstracts



TREATMENT RECOMMENDATIONS FOR MOTOR SYMPTOM CONTROL IN ADVANCED PARKINSON'S DISEASES



**ANGELO
ANTONINI**

Advanced stage of Parkinson's disease (PD) is now broader than in the past, encompassing various types and degrees of disability. It poses multiple management issues, because, despite levodopa still being unequaled in the symptomatic treatment of PD, its clinical effect tends to diminish with disease progression.

Advanced PD raises multiple management issues, as the patient carries the burden of the motor complications and non-motor symptoms making medication adjustments quite complex. Adequate control and optimal quality of life are often difficult to achieve and an integrate understanding of the pathophysiological mechanisms underlying the symptoms and of the multiple drug interactions is mandatory. While this fine balance can be generally achieved to various extents in experienced tertiary centers, mortality remains roughly unchanged, supporting thus the need for further research and therapeutic options that can truly modify PD progression and its milestones.

Motor complications tend to develop on average after four to six years of levodopa treatment. Motor fluctuations, though initially predictable, become more complex and unpredictable as the disease progresses. Dyskinesias are correlated with young age at PD onset, longer disease duration and higher LD doses. Symptoms with a poor response to LD include freezing of gait (FOG – affecting up to 80% of PD patients after 15 to 20 years of disease evolution), postural abnormalities, and dysarthria and dysphagia (present after 7 and 11 years after disease onset, respectively).

Potential risk factors for developing advanced PD have been outlined as clinical features and biomarkers. While age, sex and disease duration seem to be obvious determinants of development to advanced phase of PD, it is still debated whether the clinical phenotype at disease onset (tremor dominant, akinetic-rigid dominant, postural-instability dominant) is as predictor of PD evolution. However, other factors, among which presence of olfactory changes, rapid eye movement (REM) sleep disorders, cardiovascular autonomic dysfunction, as well as hallucinations and psychosis, may predict cognitive decline and dementia in PD, thus contributing to the overall clinical deterioration. Impulse control disorders have also been correlated with cognitive decline, particularly with executive dysfunction, as shown in one study.

Conventional therapies and routes of administration are making way for new, innovative approaches, either invasive, such as the duodenal administration of the levodopa/carbidopa intestinal gel, the apomorphine pump, or non-invasive, such as transdermal, nasal, sublingual or pulmonic routes, all intending to optimize delivery. Moreover, additional drugs like COMT and MAO-B inhibitors are required to adequately manage the full spectrum of emerging manifestations, characteristic of the advanced stage making an individualized integrated approach recommended.

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SURGICAL THERAPIES FOR PARKINSON'S DISEASE

Although the mainstay of therapy for Parkinson's disease remains medical, in the recent decades, surgery to manage intractable Parkinson's disease has gained exponential interest. Deep brain stimulation continues as the most frequently used surgical technique with significant benefit on motor and non-motor symptoms of Parkinson's disease as well as the quality of life of patients. The list of potential targets for surgery has grown and the new hardware design has enabled optimization of the therapy in the ways not envisaged even a few years back. Traditional lesioning techniques remain in use for those patients not suited for deep brain stimulation and the newer technology has increased the safety of these procedures. Interests continues in stem cell and infusion therapies although these continue to remain largely experimental in nature.



**KEYOUMARS
ASHKAN**

King's College Hospital,
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UK



COGNITIVE DECLINE IN PARKINSON'S DISEASE: THE COMPLEX PICTURE



**ROBERTA
BIUNDO**

San Camillo Hospital
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Venice, Italy

Mild cognitive impairment (PD-MCI) and dementia (PDD) are among the most frequent non-motor symptoms in Parkinson's disease. PD-MCI are six times more likely than age-matched controls to develop dementia and the PDD prevalence is 80% after 15-20 years of disease. Therefore, research has focused on the identification of early dementia biomarkers including specific cognitive at-risk profiles hoping to implement therapeutic interventions, like deep brain stimulation, when they are most likely to be efficacious. However, given the heterogeneous neuropathological, neurochemical and neuropsychological nature of cognitive deficits, definition of a comprehensive cognitive model of PDD is a challenge. Loss of nigro-striatal dopamine neurons, cholinergic projections, limbic and cortical alpha-synuclein positive Lewy bodies are associated with motor and cognitive deterioration. Although the presence of two coexisting cognitive profiles in PD is consistently reported across studies, evidence also suggests that each clinical, neuropsychological and MRI assessments cannot by themselves reliably discriminate PD patients who are likely to progress to dementia. Prospective studies combining neuroimaging and sensitive cognitive tests, should clarify the interplay between the various neurodegenerative processes, and the contribution of structural disconnections in brain functional networks, heralding the development of dementia. We suggest that additional pathology plays a role in the early development of dementia and this includes β -amyloid deposition possibly in specific brain regions. Finally, the MMSE, although relatively insensitive in detecting cognitive abnormalities in the early phases of PD but it shows a rapid decline in presence of dementia, maybe a valuable cognitive biomarker to identify patients at risk for dementia.



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GENETICS OF PARKINSON'S DISEASE



**VINCENZO
BONIFATI**

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In the past twenty years there has been substantial progress in our understanding of the genetic factors involved in the etiology and pathogenesis of Parkinson's disease (PD).

Highly-penetrant mutations in different genes (e.g. SNCA, LRRK2, VPS35, Parkin, PINK1, and DJ-1) are known to cause rare monogenic forms of the disease.

Furthermore, different variants with incomplete penetrance in the LRRK2 and the GBA gene are strong risk factors for PD, and are especially prevalent in some populations.

Last, common variants of small effect size, modulating the risk for PD, have been identified by genome-wide association studies in more than 20 chromosomal loci.

In this lecture, I first outline the evolution of the research strategies to find PD-related genes, and then focus on recent advances in the field of the monogenic forms.

Additional genetic determinants of PD likely remain to be identified, as the currently known mutations and variants only explain a minor fraction of the disease burden.

There is great expectation that the new DNA sequencing technologies (exome and whole-genome sequencing) will bring us closer to the full resolution of the genetic landscape of PD.



EYE MOVEMENT ABNORMALITIES IN PATIENTS WITH MOVEMENT DISORDERS

Eye movement abnormalities in patients with movement disorders often aid to the final clinical diagnosis. There is a good clinical-localization correlation between eye signs and structures affected and, furthermore, the simple bed-side examination is sufficient for diagnosis in the vast majority of patients. In PSP the cardinal abnormality is saccadic slowing, particularly vertical, and often leading to the typical vertical supranuclear gaze palsy. In MSA the useful abnormalities are related to the underlying cerebellar dysfunction in this condition: broken pursuit, VOR suppression, positional down-beat nystagmus and saccadic dysmetria. In CBD the main abnormalities are of an apraxic type, with patients experiencing difficulties in shifting the eyes from one target to another (i.e. delayed saccadic eye movements). These abnormalities will be demonstrated with video images.



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DYSTONIA TREATMENT



**IORELLA
CONTARINO**

Haga Teaching Hospital
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Appropriate dystonia treatment relies on an accurate diagnosis and disease characterization. Some forms of dystonia require specific treatment, for example dopa-responsive dystonia or dystonia occurring in the context of other neurodegenerative disorders. In addition, the therapeutic approach to generalized dystonia differ from that for focal or segmental dystonia.

Therapeutic treatments for dystonia encompass pharmacological therapies, botulinum toxin injections (BoNT), surgical interventions and supportive treatments.

Oral medications include anticholinergic agents (particularly trihexyphenidyl), GABA-mimetic agents, dopamine receptor antagonists, and benzodiazepines (especially diazepam and clonazepam). In many cases the efficacy of these drugs is unsatisfactory and limited by side-effects. Trihexyphenidyl is the most used agent, but the tolerance profile is low especially in adult patients. Benzodiazepines are often effective in reducing dystonia-related pain, anxiety and dystonic tremor. Gaba-mimetics such as baclofen are mainly indicated in case of coexistent spasticity.

Local injections of botulinum neurotoxin (BoNT) are currently the treatment of choice for focal dystonia. BoNT type A is the most frequently used; type B is only proposed in selected cases. Although BoNT treatment is widely applied worldwide, many questions remain open in clinical practice.

In those with unsatisfactory response to medical treatment, surgery may be considered. Surgical options include peripheral surgery, pallidotomy, or deep brain stimulation. Peripheral surgery, such as selective peripheral denervation, can provide improvement in about two-thirds of cases, with frequent relapses, and is now rarely performed. Deep brain stimulation (DBS) of the Globus Pallidus pars interna appears to be a better choice, despite potential severe complications. Alternative DBS targets, such as the subthalamic nucleus, need further investigation.

Evidence on the effectiveness of allied care treatments, including physiotherapy and cognitive behavioural therapy, is scanty.



ISSUES IN THE DOPAMINE AGONISTS' TREATMENT IN PARKINSON'S DISEASE



**CRISTIAN
FALUP-
PECURARIU**

Dopamine agonists (DA) were developed to provide continuous dopaminergic stimulation. However, there are a couple of side effects or situations that could challenge the practitioner.

By using clinical cases it will be shown different issues in the use of dopamine agonists: gastrointestinal problems, side effects with the necessity to switch from one dopamine agonist to another, with maintaining motor control, correct doses in early and advanced diseases.

Transdermic system of DA delivery in PD has the benefit to avoid gastric emptying problems and has a stable plasma level with one single day administration.

Recent data suggest that the gastrointestinal disturbances are present in 45% in Hoehn Yahr stage I and 73% in stage IV. Partial gastric emptying, reduced gastric emptying and constipation are the most prevalent GI symptoms. GI disturbances are triggered due to PD and not due to increased age. Hence, gastroparesis may be a contribution to the complex etiologies of motor fluctuations.

There is a direct dose-response relationship for some DA, according to the mean change in UPDRS II & III scores.

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SEXUAL DYSFUNCTION IN PARKINSON'S DISEASE



**SHARON
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Movement Disorders
Institute

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Sackler Faculty of
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Israel

Sexual dysfunction (SD) is common in the general population, particularly in the elderly, but more so in patients with Parkinson's disease (PD). SD is an important nonmotor symptom that likewise affects young PD patients. It includes decreased sexual desire, inability to maintain an erection, premature or impaired ejaculation and difficulty to achieve an orgasm in males and decreased sexual desire, vaginal tightness, loss of lubrication, involuntary urination, anxiety, inhibition and dissatisfaction in females.

As sexual functioning depends on motor performance it may be affected by motor problems such as muscle rigidity, bradykinesia, tremor and dyskinesia, depending on the motor state of the patient and dopaminergic medication schedules. Autonomic disturbances affecting sphincter control may cause discomfort and limitations. Sleepiness and fatigue may minimize opportunities for sexual activity. Depression and apathy may cause decreased desire and their treatment with antidepressants can contribute to erectile dysfunction and delayed orgasm.

While animal studies have suggested that dopamine promotes sexual motivation, copulatory proficiency and genital reflexes by acting in various integrative brain areas, such as the medial preoptic area, the paraventricular nucleus and the nucleus accumbens, its importance in sexual functioning in humans is still a matter of debate.

In summary: several variables should be considered when evaluating SD including physical, psychological, neurobiological and pharmacological aspects that commonly interact and merge becoming hardly distinguishable.

All these as well as treatment approaches will be discussed in this review lecture.



NON-DOPAMINERGIC APPROACHES TO TREATING PARKINSON'S DISEASE



PETER JENNER

Neurodegenerative Diseases Research Group, Institute of Pharmaceutical Sciences, Faculty of Life Sciences and Medicine, King's College London, UK

The pathology of Parkinson's disease is widespread affecting many non-dopaminergic areas of the brain and involves multiple neurotransmitters. Within the basal ganglia, loss of the nigro-striatal pathway alters the activity of the strio-thalamo-cortical loops and the many neurotransmitters systems that contribute to its function. These changes in non-dopaminergic systems offer the opportunity for the development of non-dopaminergic drug therapy for the treatment of both motor and non-motor symptoms of PD, for the use of multimodal molecules that affect a range of different neurotransmitter systems and for repurposing drugs from other therapeutic areas that influence non-dopaminergic neuronal pathways affected in PD.

Non-dopaminergic therapy for motor symptoms and the treatment of dyskinesia has been used in PD for many years in the form of the weak NMDA antagonist amantadine and anticholinergics. New approaches to glutamatergic treatment are being investigated but commonly the therapeutic window is narrow and side-effects limit use in man. New antimuscarinic drugs are being developed with an understanding of the role of the M4 receptor subtype found in basal ganglia. Serotonergic agonists and antagonists are proving useful in controlling dyskinesia in preclinical studies and are under clinical investigation. Based on these types of findings, many optimistic reviews of the use of non-dopaminergic drugs in PD have appeared but there has been a lot of failure of these types of molecules to translate from the laboratory to effect in clinical trial. One example is the A2a adenosine antagonists but here clinical trial design might be at least partial responsible for the failure.

Non-motor symptoms of PD are largely non-dopaminergic in nature but the precise pathophysiology is not yet understood. Non-dopaminergic drugs are routinely used on a symptomatic basis to treat non-motor symptoms of PD. There are few drugs specifically developed for non-motor symptoms. One exception is the 5-HT antagonist, pimavanserin for the treatment of psychosis. A range of other molecules are currently in clinical trial for both central and peripheral non-motor symptoms of PD and the results are eagerly awaited. However, the preclinical science of non-motor symptoms of PD is well behind the clinical characterisation and effective animal models of non-motor symptoms are required. Existing models of PD do show non-motor symptoms and these are being increasingly characterised to provide a pharmacological test bed for novel treatments.

Lastly, there is a need for single drugs with a range of pharmacological actions to treat multiple symptoms in PD so lowering the pill burden. These would previously have been deemed to be 'dirty' drugs but are now termed as having 'a rich pharmacology' or being 'multimodal'. There are so far few examples but a good illustration would be the repurposing of the antiepileptic, zonisamide which has both GABAergic and dopaminergic properties and the recently introduced reversible MAO-B inhibitor safinamide which has interesting channel blocking actions.



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EPIDEMIOLOGY OF PARKINSON'S DISEASE



MEIKE KASTEN

Department of
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and Institute of
Neurogenetics
University of Lübeck,
Germany

The Epidemiology of Parkinson disease (PD) encompasses descriptive and analytical epidemiology, in other words the description of disease frequency and the analyses of factors contributing to disease risk. A recent study from Portugal reported a PD prevalence of 0.24% in the population aged 50 years and above. PD prevalence increases with age and shows sex and regional differences worldwide. Similarly, PD incidence increases with age and is higher in men than women. Thus, age, sex and possibly ethnicity act as risk/protective factors for PD. Additional risk factors include family history, certain genetic variants and several environmental risk factors such as head injury or pesticides and protective factors such as smoking, coffee drinking, or physical activity. The investigation of descriptive and analytical epidemiology is complicated by bias, confounding and reverse causation. Furthermore, it is likely that different risk factors interact such as head injury and expansion of Rep1 in alpha synuclein (gene-environment interaction). It is likely that gene-gene and environment-environment interactions are also important. The challenge of reverse causation in PD is emphasized by the long preclinical period and the likely existence of several preclinical stages, e.g. the premotor phase. Thus, it remains elusive whether e.g. depression or constipation are risk factors or prodromal markers of PD.



REHABILITATION IN PARKINSON'S DISEASE



**DAFIN F.
MUREȘANU**

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The current therapies available in the Parkinson disease are symptomatic and, in time, they become less efficient, due to the progression of the subiacent pathological process. The discovery of certain agents that contribute to the protection of neurons from cellular injuries, induced by different biochemical elements, associated with diseases pathogenesis, and that cause the illness to slow or to stop, becomes thus a priority.

The progresses in understanding the pathogenetic mechanisms that bring along the death of the nigric cells, offer new data, suggesting that the intervention possibilities in the oxidative stress, in the processes of mitochondrial disfunction, in the processes of excitotoxicity, of degrading the proteins and apoptosis, could be beneficial.

The studies in vitro and on animals, attribute to the monoaminoxidasis inhibitors (selegiline and rasagiline), to medications with anti-toxic excitating effect (rilusoles), bioenergetic factors (Q10 coenzyme), trophic factors and anti-apoptotic medication, the role of potential neuroprotection agents. In spite of all these, the final proofs of a neuroprotection are missing.

As our clinical knowledge on Parkinson's disease is far to be completed, the probability of identifying a neuroprotection medication increases, but this aspect raises the need for new studies.



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PUMP-BASED THERAPIES FOR ADVANCED PARKINSON'S DISEASE



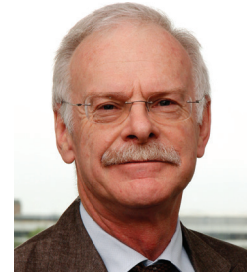
PER ODIN

Dept of Neurology, Skåne University Hospital, Lund, Sweden and Central Hospital Bremerhaven, Germany

Continuous drug delivery (CDD) and continuous dopaminergic stimulation (CDS) have been shown to have advantages concerning reduction of motor fluctuations and dyskinesias, in animal models as well as in clinical studies in patients with Parkinson's disease (PD). In advanced PD CDD is presently provided with apomorphine infusion subcutaneously with portable pumps (AI) or intraintestinal infusion of levodopa-carbidopa gel (LCIG) with portable pumps. Clinical studies have demonstrated that AI and LCIG both reduce the "off" time with 60-65% in patients with motor fluctuations. Both treatments also reduce the time with and the intensity of dyskinesias. Also concerning non-motor symptoms pump therapy can induce improvements; this concerns for example sleep, mood, urological and gastrointestinal symptoms. In total most patients who switch to pump therapy get an improvement of health-related quality of life. The most common side effect with AI is a nodule formation—local inflammation—in the skin at the infusion point. This is normally a small problem, but can in some cases lead to termination of the therapy. With LCIG the most common complications are connected to the establishment of the PEG and to the infusion equipment. The main indication for pump therapy is motor fluctuations and/or dyskinesias in spite of optimized peroral/transdermal therapy, but non-motor symptoms can be part of the indication. Contraindication for pumps is mainly when there is no or little L-dopa effect and when the pump cannot be handled in an adequate way. Several new pump-based therapies for PD are presently under development.



PATHOPHYSIOLOGY OF RESTLESS LEGS AND AUGMENTATION



WALTER PAULUS

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Göttingen, Germany

In restless legs syndrome (RLS) pathophysiological data converge on the hypothesis of a complex network sensorimotor disorder involving cortical, subcortical, spinal cord, and peripheral nerve generators, resulting in an enhanced excitability and/or decreased inhibition. Multiple mechanisms, such as reduced central inhibition and abnormal peripheral nerve function, contribute to the pathogenesis of RLS similarly to some chronic pain conditions. Dopamine transmission dysfunction, either primary or triggered by low iron and ferritin concentrations, may also bridge the gap between RLS and chronic pain entities. When ferritin is low or anemia is present, iron formulations can be effective but are not yet approved for RLS therapy. In general, initiation of therapy is recommended with dopamine agonists (pramipexole, ropinirole or rotigotine transdermal patch), in the US and Japan also with the approved gabapentin enacarbil. Other α -2-ligands studied to be effective in RLS are gabapentin or pregabalin. For second line therapy, if other medication failed or are no longer effective, opioids (prolonged release oxycodone–naloxone, approved in Europe) are also recommended for severe RLS. The major complication of dopaminergic therapy consist of augmentation; a worsening of RLS severity and occurrence of symptoms earlier during the day after successful dopaminergic medication has started. Pulsatile dopaminergic agents and high dosages over time are possible risk factors of augmentation. Management of augmentation may include reducing dopaminergic dosage, switching to a less pulsatile acting dopamine agonist or to an opioid, or both.



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SPEECH AND VOICE IMPAIRMENT IN PARKINSON'S DISEASE



**LĂCRĂMIOARA
PERJU-
DUMBRAȚĂ**

University of Medicine
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"Iuliu Hatieganu"
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One of the characteristics Parkinson's disease (PD) is amendment of speech and voice, leading to impaired communication. Almost all of untreated PD patients express speech and voice defects characterized by hypophonia, dysprosodia, imprecise consonants, dysrhythmia, tachyphemia, dysfluency and voice tremor. Functional MRIs performed during voice reading tasks suggests that speech declines earlier than gait.

PD speech and voice impairment are due mainly by affecting motor systems modulating speech, respiration, phonation, sounds articulation and prosody. Speech and voice impairment etiology is both dopaminergic and non-dopaminergic and is not yet fully understood, which makes conventional treatment options used to treat PD not very effective regarding speech.

The clinical evaluation should cover spontaneous speech and its stimulability by using maximum performance tests. The severity of speech impairment is recommended to be rated using dysarthria subscale of the Therapy Outcomes Measures. Speech evaluation tests involve perceptual assessment (repetition of syllables, groups of letters), acoustic analyses (fundamental frequency, jitter, shimmer, voice onset time, maximum phonation time, etc.) or physiologic measures (laryngeal electromyography, videolaryngostroboscopy, kinetic measurements of the tongue, lips, jaw and respiratory movements).

The most important therapeutic approaches include voice therapy, Levodopa and deep brain stimulation. Voice therapy methods (Pitch Limiting Voice Treatment and Lee Silverman Voice Therapy) aims to increase phonatory-respiratory effort for raising motor output amplitude during speech. The effects on speech of deep brain stimulation of the subthalamic nucleus and Levodopa are inconsistent and inconclusive. Levodopa apparently enhances respiratory control, loudness, prosody and intelligibility and not cueing and feedback mechanisms. Deep brain stimulation can worsen speech production, particularly high-frequency stimulation can lead to respiratory over-drive and high incentives of vocal fold enclosure.

Subtle changes in speech and voice of patients may have an effect on patient quality of life, which emphasize the importance of early referral to a speech-language pathologist.



NEUROIMAGING IN MOVEMENT DISORDERS



MARIOS POLITIS

Over the past three decades, neuroimaging studies—including structural, functional and molecular modalities—have provided invaluable insights into the mechanisms underlying Parkinson disease (PD). Observations from multimodal neuroimaging techniques have indicated changes in brain structure and metabolic activity, and an array of neurochemical changes that affect receptor sites and neurotransmitter systems. Characterization of the neurobiological alterations that lead to phenotypic heterogeneity in patients with PD has considerably aided the in vivo investigation of aetiology and pathophysiology, and the identification of novel targets for pharmacological or surgical treatments, including cell therapy. Although PD is now considered to be very complex, no neuroimaging modalities are specifically recommended for routine use in clinical practice. However, conventional MRI and dopamine transporter imaging are commonly used as adjuvant tools in the differential diagnosis between PD and nondegenerative causes of parkinsonism. First-line neuroimaging tools that could have an impact on patient prognosis and treatment strategies remain elusive. This talk discusses the lessons learnt from decades of neuroimaging research in PD, and the promising new approaches with potential applicability to clinical practice.

Neurodegeneration
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DIAGNOSTIC APPROACH TO PATIENTS WITH DYSTONIA

Dystonia is a hyperkinetic movement disorder characterized by sustained or intermittent muscle contractions causing abnormal, often repetitive movements, postures, or both. Dystonic movements are typically patterned and twisting, and may be tremulous. Dystonia is often initiated or worsened by voluntary action and associated with overflow muscle activation. Based on the new classification, dystonia is characterized along 2 axes: a) clinical characteristics; including age at onset, body distribution, temporal pattern and associated features (additional movement disorders or neurological features); and b) etiology; including nervous system pathology and mode of inheritance. Since dystonia may be present in numerous neurological and other disorders, proper understanding of its clinical and other characteristics may significantly facilitate reaching the proper diagnosis. This lecture will highlight differentiation of dystonia from other movement disorders, utilization of the new classification of dystonia in everyday clinics, highlight the most important dystonia syndromes and especially treatable conditions associated with dystonia and conclude with interactive case reports discussed with the audience.



**MATEJ
SKORWANEK**

Safarik University and
University Hospital of
L. Pasteur
Kosice, Slovakia



THE IMPORTANCE OF AN EFFECTIVE TREATMENT: PRACTICAL CONSIDERATION



**FABRIZIO
STOCCHI**

University and IRCCS
San Raffaele, Rome,
Italy

The approach to early Parkinson's disease denotes the communication of the diagnosis and important decisions, such as when and how to start treatment. Today there is a large debate about the opportunity to start pharmacological treatment as soon as the disease manifests. The theory of an early compensatory effect of symptomatic drug with an associated better long-term symptom control is fascinating. Moreover, the long-term follow-up of two pivotal trials one with rasagiline and one with rotigotine seems to support this hypothesis. The other decision that the physician must take is about the drug to use in an untreated patient. Evidence based medicine and guidelines indicate which drugs have robust evidence of efficacy and tolerability in this specific population. However, *de novo* patients may show different characteristics and they may be in a different phase of their disease. MAOB-I monotherapy can be efficacious but only in the very early stage. DA agonists are efficacious in early PD they can improve motor and non-motor symptoms and delay motor complications. Certainly, DA agonists can be added to levodopa instead of increasing the levodopa dose, for reducing the risk of dyskinesia. Patients on DA should be monitored to avoid the appearance of possible side effect such as impulse control disorders even if recent studies showed that rotigotine bring less risk of ICD compared to other DA. Levodopa remain the most effective drug but it is limited by its short half-life. Slow release formulations introduced in late eighties are not very efficacious and their effect is unpredictable. Levodopa should be used at minimal efficacious dose to reduce the risk of fluctuations and dyskinesia. The *de novo* population is very heterogeneous and the decision about the drug initially should take into account the general characteristics of the patient, such as age, cognitive status, comorbidities, occupation, and the most affected side (dominant or non-dominant) but also of the severity of the symptoms and the presence of non-motor symptoms. Today a combination of drugs rather than using a single drug at high dose may be considered.



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RBD - SYMPTOMATOLOGY, ASSESSMENT AND IMPLICATIONS FOR PARKINSON SYNDROMES



**CLAUDIA
TRENKWALDER**

University Medical
Center Goettingen,
Paracelsus-Elena-Klinik
Kassel, University of
Goettingen, Germany

Parasomnias are movement disorders in sleep that can occur either in REM sleep or in NON-REM Sleep. For neurologists, especially the REM-Parasomnias (REM-sleep behavior disorder, RBD) are interesting, as they are possible prodromal features of neurodegenerative diseases. Idiopathic RBD is defined by the International Classification of Sleep Disorders in its current 2014 version (ICSD-3).

RBD is characterized by either mild jerky, or violent movements of the extremities occurring in REM sleep, associated often with nightmares. Patients with idiopathic RBD can fall out of bed or even hurt their bedpartner without memorizing the event in the next morning. Examples of RBD characterized by vocalizations, jerky movements of the extremities or the whole body, bed falls or complex movements are shown in videos taken from REM sleep PSG. Typically vocalizations are associated with motor events and the spectrum goes from murmuring, talking and laughing up to screaming. In the polysomnography an increased muscle tone of the chin during REM sleep with phasic and tonic activities can be recorded, and is defined according to ICSD-3 criteria and Frauscher et al. (2012).

RBD is now recognized as a prodromal state of neurodegenerative diseases associated with misprocessing of intracellular alpha-synuclein, thus facilitating the identification of an at-risk population. This hypothesis originates from long-term observations of spectacular, violent RBD cases in sleep centers, when patients fall out of bed during REM sleep episodes and develop a Parkinson syndrome up to 18 years later (Schenck et al 2013).

In clinically manifest PD, several studies have shown an association between RBD and a more severe course of the disease, cognitive impairment, postural instability and increased autonomic failures. Our own data from a large cohort of PD patients in various stages of the disease support the concept that RBD precedes a more advanced stage of neurodegeneration, suggesting RBD as a possible clinical progression marker (Mollenhauer et al 2013). Several prodromal signs of RBD can be observed in de novo PD populations, such as small jerky movements during REM sleep, defined as REM-Behavioral Events (RBE), associated with dreaming contents, that may be defined as prodromal RBD (Muntean et al 2015).

References

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Mollenhauer B, Trautmann E, Sixel-Doring F, et al. Nonmotor and diagnostic findings in subjects with de novo Parkinson disease of the DeNoPa cohort. *Neurology* 2013;81:1226-34.

Muntean ML, Trenkwalder C, Walters AS, Mollenhauer B, Sixel-Doring F. REM Sleep Behavioral Events and Dreaming. *J Clin Sleep Med* 2015.



Biographies



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ANGELO ANTONINI

/Italy

Angelo Antonini, MD, PhD is director of the Parkinson Unit at the Institute of Neurology, IRCCS San Camillo Hospital in Venice and Professor at the University of Padua.

He earned his medical degree from the Università degli Studi di Roma 'La Sapienza', Rome. In November 1990 he completed his neurology training with honors and then undertook a visiting fellowship at the PET Department Paul Scherrer Institute, Villigen, Switzerland before starting his PhD in neuroradiology under the supervision of Professor Klaus Leenders. In February 1995 he was promoted to Associate Professor of Neurology at the New York University and worked at the Neuroimaging laboratory of the North Shore University Hospital, NY directed by David Eidelberg. In November 1997 he moved to the Parkinson Institute in Milan where coordinated Clinical Research at the Department of Neuroscience until March 2009.

His research focuses on pharmacology of dopaminergic medications, neuroimaging as well as cognitive and behavioral aspects of Parkinson's disease, multiple system atrophy, PSP and other movement disorders. In addition he is actively involved in the use of continuous infusion of levodopa and apomorphine as well as deep brain stimulus (DBS) for the treatment of motor complications in advanced Parkinson e dystonia patients.

During his academic career he has received several awards, published more than 300 peer-reviewed manuscripts and several book chapters. He serves as reviewer for the main neurology journals. He is the Chair of the European Education Committee of the Movement Disorders Society, Treasurer of the Association of Parkinsonism and Related Disorders and Secretary of the Italian Parkinson and Movement Disorders Association LIMPE.



KEYOUMARS ASHKAN

/UK

Prof Ashkan qualified from the University of Wales College of Medicine in 1993 with commendations. He then underwent dual postgraduate training in medicine and surgery, obtaining both the Fellowship of the Royal College of Physicians (FRCP) and the Fellowships of the Royal College of Surgeons of England and Glasgow (FRCS). He completed his higher specialist training in neurosurgery in London, followed by subspecialist training in Stereotactic and Functional Neurosurgery with Prof Benabid in France leading to a higher Doctorate degree in research.

Professor Ashkan is the lead for Functional and Oncological Neurosurgery at King's College Hospital, University of London since 2004. His clinical practise covers the 4.5 million population of South East London and Kent, translating into 300-350 operations per year. He heads the Neurosciences Clinical Trial Unit at King's and is the Deputy Lead for the King's Neurosciences Research Advisory Group. He is the President of the British Society for Stereotactic and Functional Neurosurgery. He is also the Chairman of the Neurosurgical section of the International Parkinson and Movement Disorders Society. He is the Lead for Genomics England's Brain Tumour Programme.

Prof Ashkan's main clinical and research interests are neuro-modulation, especially adult and paediatric deep brain stimulation, surgical management of pain, and neuro-oncology. He has won over 20 undergraduate and postgraduate prizes and scholarships. He has attended/ chaired/ presented papers in over 250 national and international meetings and published over 360 full papers, abstracts and book chapters. To date he has been Chief/ Principal Investigator in over 15 major studies/ trials, including the UK Chief Investigator of deep brain stimulation in depression and European Chief Investigator for immunotherapy for brain tumours.



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OVIDIU BĂJENARU
/Romania

1983 : M.D. at the Faculty of Medicine of University of Medicine and Pharmacy
"Carol Davila" Bucharest

1983-1985 : post graduate hospital stagium in University Hospital of Emergency Bucharest

1985- 1989 : resident of neurology

1985 : assistant professor – University of Medicine and Pharmacy "Carol Davila"
Bucharest- Department of Neurology of the University Hospital of Emergency Bucharest

1989 : specialist in neurology, confirmed by the Ministry of Health of Romania

1993 : Ph.D. at the University of Medicine and Pharmacy "Carol Davila" Bucharest
- senior lecturer of neurology
- Head of Department and Medical Chief (University Hospital of Emergency, Bucharest

1994 - 1999 : Associate Professor of Neurology

1999 (since) : Professor of Neurology at the University of Medicine and Pharmacy
" Carol Davila" Bucharest and Chairman of the Neurology Department of the
University Hospital of Emergency Bucharest

2006: : Doctor Honoris Causa - University „Ovidius” – Constanta (Romania)

2011 : Director of Department of Clinical Neurosciences - University of Medicine and
Pharmacy " Carol Davila" Bucharest

2013 (since) : Corresponding member of the Romanian Academy of Medical Sciences

2016 (since) : Corresponding Member of the Romanian Academy

Other professional activities :

2000-2004 : Vice-Dean of the Faculty of Medicine - University of Medicine and Pharmacy
"Carol Davila" Bucharest

2001-2013 : President (founder) of the Romanian Society of Neurology

2013(since) : Honorary President ad vitam of the Romanian Society of Neurology

2007 (since) : Representative of Romania in UEMS – European Board of Neurology (EBN);

2010-2015 : Secretary of the Executive Committee of UEMS-EBN

2003-2009 : member of the Scientific Committee of ECTRIMS

2005-2009 : member of the Executive Committee of the European Society of Neurology

Post graduate training :

1992 - - 1994 : post graduate training in clinical neurology and functional investigations of the
nervous system at University " Rene Descartes"(Paris) : C.H.U. Sainte-Anne
(Neurology) and C.H.U. Cochin – Port Royal (Functional Investigations of the
Nervous System) and training in neuroendocrinology

1997 : assistant of clinical research in pharmaco-clinical trials (Paris)

2009, 2011,2015,2017: International training for methodology in clinical research

Fields of interest for the scientific research

- dementia and neurodegenerative diseases (in particular Parkinson's disease)
- multiple sclerosis
- stroke
- experimental and clinical study of sleep disturbances in the neurological and neuroendocrinologic diseases



- more than 450 scientific paper ISI Web of Science – indexed, with over 2500 citations published and reported in different national and international scientific meetings
 - ISI Web of Science: Hirsch index=16
- author or co-author for 14 medical books and monographs (published in Romania)
- co-author (1 chapter/each volume) in 2 international handbooks of Neurology
- Country Principal Investigator – in more than 30 international, multicentric clinical trials
- Principal Investigator of the research site – in more than 30 international and national multicentric trials
- Member of the Steering Committee of more international clinical trials
- More national grants of research

Other activities:

- coordinator of the Continuous Medical Education (EMC) national program of the Romanian Society of Neurology for neurologists in Romania (2001 – 2014)
- coordinator and author of the Guidelines for diagnosis and treatment of neurological diseases (agreed by the College of Medecins of Romania) main author of the national guidelines for Parkinson's disease, Multiple Sclerosis and Dementia
- coordinator of the National Program of the National House of Insurance and Ministry of Health, for treatment of patients with neurological diseases (2000 - 2015)
- initiator and coordinator of the national program for interventional revascularization treatment in acute stroke and development of stroke units in Romanian hospitals
- initiator and coordinator of the first medical team in Romania for DBS and other interventional treatments in advanced Parkinson's disease and dystonia
- 2002-2016 chief-editor of Romanian Journal of Neurology (the official journal of the Romanian Society of Neurology); since 2016 – Honorary Chief Editor
- chairman and main organiser of the Annual National Congress of the Romanian Society of Neurology (since 2001) and othe national and regional neurological scientific meetings
- member of the Faculty for more annual editions of the International Congress of Controversies in Neurology, International Congress of Vascular Dementia, International Annual Meetings of the Society for the Study of Neuroprotection and Neuroplasticity and other international scientific neurological meetings
- co-chairman of the annual International Summer School of Neurology organised since 2005 in Eforie Nord (Romania) and other international teaching courses in Parkinson's disease and Multiple Sclerosis
- invited lecturer of the World Federation of Neurology for international teaching courses in Vietnam (2012) and Kazakhstan (2015)

Scientific affiliation:

- Romanian Society of Neurology (Honoray President ad vitam)
- UEMS – European Board of Neurology (Secretary of the Executive Committee between 2010 - 2015)
- European Neurological Society (ENS) – member of the Executive Committee between 2005 – 2009
- European Stroke Organization
- European Federation of Neurological Societies (EFNS) and European Academy of Neurology (since 2014)
- American Academy of Neurology (coresponding member)
- Danube Neurological Association (Vice-Secretary General – elected in 2011)
- ECTRIMS (member of the Scientific Council 2003-2009)
- other 6 prestigious international scientific societies



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- 2005, 2006, 2010, 2011, 2016: awarded by the Prize of Excelency in Neurology for the scientific activity in Romania
- 2008: awarded by the Romanian Society of Internal Medicine for the best scientific activity in a related medical speciality
- 2014: awarded by the International Brain Network Foundation and Romanian Academy of Medical Sciences, for excellency in the development of management of patients with multiple sclerosis in Romania
- 2015:
- awarded by the Romanian Ministry of Health by the Prize of Excelency in Neurology
 - awarded by the "Acad. Marin Voiculescu Foundation" by the Prize of Excelency in Neurology
 - awarded by the Romanian Orthodox Patriarchy by the Order "Saint Emperors Constantin and Elena" for excellency in the medical national care system



ROBERTA BIUNDO

/Italy

Roberta Biundo is currently working as a neuropsychologist at the “San Camillo Hospital Foundation”, I.R.C.C.S., Venice, Italy. She was awarded a Ph.D. in Neuroscience, EU Marie Curie Network, at the University of Hull (UK) exploring preclinical indicators of abnormal cognitive decline in ageing (2010). Previously, she was awarded a Marie Curie fellowship as research assistant at the University of Hull, (UK) (2007) where she investigated deterioration of language skills in patients with neurodegenerative brain diseases using experimental neuropsychological assessment, structural neuroimaging techniques as well as computerized assessments. She was awarded a fellowship to The Vivian Smith Advanced Studies Summer Institute of the Neuropsychological Society at Xilocastro (Greece) (2006) and obtained a master in Neuropsychology Across the Lifespan. She graduated with honors in Experimental Psychology at the University of Trieste (Italy) (2004) and underwent psychology training in Cognitive Psychology and Behavior analysis completing her psychologist training in Trieste (2005). Her main research focus is investigation of the interplay between cognitive-behavioral deficits, genetic variability, and neuronal substrates associated with Parkinson’s disease, atypical parkinsonisms and Huntington’s disease using neuroimaging techniques (e.g., MRI, fMRI, and cortical thickness). She also indentified indicators of neurorehabilitation treatment efficacy (cognitive training plus t-DCS) that may have prognostic value at the stage of mild cognitive impairment. She is involved in different multicenter study groups: 1) Multicenters longitudinal cohort-study in Lewy-body dementia (DLB): she leads the feasibility of cognitive test in detecting cognitive decline over time; 2) Validation of the Movement Disorders Society criteria for mild cognitive impairment in Parkinson’s disease (PD-MCI); 3) Retrospective and longitudinal cohort studies in Multisystem Atrophy (MSA): Develop strategies for definition of dementia in MSA patients. She is currently working at developing strategies for defining cognitive high risk profile in Parkinson dementia and Dementia with Lewy Bodies. She also keen to develop valid global cognitive scales to detect high risk profile for Parkinson dementia. Moreover she actively working in better clarifying the dementia profile in MSA patients. Finally she is working at developing guidelines and detailed protocol recommendations for cognitive tests that may best detect cognitive decline over time in different movement disorders.



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VINCENZO BONIFATI
/The Netherlands

Vincenzo Bonifati received his MD in 1988 from La Sapienza University, Roma, Italy. In 1992 he completed his residency in neurology there, and was appointed staff neurologist. After several years dedicated to the clinical care of patients with Parkinson's disease and other movement disorders, in 2000 he moved to the Erasmus University Rotterdam, where he received his PhD in human molecular genetics in 2003. In 2006 he was appointed Associate Professor, and in 2012, Professor of Genetics of Movement Disorders.

His research focuses on understanding the molecular mechanisms of Parkinson's disease (PD) and finding novel therapeutic targets, by the identification of highly-penetrant disease-causing genetic mutations, and the characterization of the involved molecular pathways. For additional information please see the website: http://www.erasmusmc.nl/klinische_genetica/research/introduction/bonifati/

Over the past 15 years he built an international network for the study of families with PD, case-control series, and genetically isolated populations (including Sardinia). The combination of strong clinical and molecular genetic expertise has been a key factor in his research endeavor.

His work led to the discovery of different, novel forms of hereditary parkinsonism, such as PARK7, PARK15, and recently, PARK20. He also described the Gly2019Ser mutation and the Gly2385Arg variant in the LRRK2 gene, considered among the most relevant genetic determinants of the common forms of PD. He identified the first inherited disorder of manganese transport in man, caused by mutations in the SLC30A10 gene, and characterized by dystonia or parkinsonism and multi-organ disturbances.

In 2015, he published the first large-scale exome study of PD, nominating several novel candidate risk-genes for the disease. He recently published (2016) mutations in the DNAJC6 gene causing a novel form of earlyonset PD.

He published more than 170 papers in peer-reviewed journals, and has an H-index of 54.

He is the Associate Editor for Europe of Parkinsonism & Related Disorders, and the Section Editor for Genetics of Current Neurology and Neuroscience Reports. He is currently an Editorial Board member of Neurogenetics, Basal Ganglia, and Journal of Parkinson's disease, and has served in the Editorial Board of Movement Disorders.

He is regularly invited to give lectures at international congresses, and is currently member of the scientific organizing committees of the two world-class congresses for PD and other movement disorders: the International Congress on the Parkinson's disease and Movement disorders Society (IPMDS), and of the International Association for Parkinson's disease and Related Disorders (IAPRD).



ADOLFO BRONSTEIN

/UK

Adolfo Bronstein is Professor of Clinical Neuro-otology at Imperial College London and a Consultant Neurologist at Charing Cross Hospital and at the National Hospital for Neurology and Neurosurgery, Queen Square, London. He heads the Neuro-otology Unit in the Division of Brain Sciences at Imperial College. He has written over 250 papers on clinical and basic aspects of eye movements, balance and spatial orientation. His book, 'Dizziness' received a 'High Commendation' at the 2008 BMA Medical Book prize Competition. Prof Bronstein is an enthusiastic teacher of neuro-otology and balance disorders in European and world neurological societies. In 2008 he obtained the Nylen-Hallpike Prize of the Barany Society for outstanding contribution to clinical neuro-otology. His current research interests are the high order mechanisms involved in central compensation of peripheral vestibular disorders as well as the role of small vessel white matter disease in balance dysfunction in the elderly. He was the first chairman of the British Society of Neuro-otology and has been chairman of the neuro-otology panel for the European Federation of Neurological Sciences and president of the clinical neuroscience section of the Royal Society of Medicine.



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K. RAY CHAUDHURI
/UK

Professor K Ray Chaudhuri is the Clinical Director of the National Parkinson Foundation International Centre of Excellence at King's College and Kings College Hospital London, Lead of the King's Neuroscience Research and Development unit and Chairman of the Movement Disorders Society Non-motor Study Group at Denmark Hill Campus in London.

Professor Ray Chaudhuri also sits on the Nervous Systems Committee of the UK Department of Health, National Institute of Health Research, and serves as a member of the Scientific Programme Committee of the International Parkinson's and Movement Disorders Society. In addition, he serves as a member of clinical advisory groups to Parkinson's UK and the European Parkinson's Disease Association. Having published over 350 papers and co-edited 4 books on PD and restless legs syndrome, Professor Ray Chaudhuri currently serves on the editorial board of numerous international journals including Basal Ganglia, the Journal of Parkinson's Disease and is the editor in chief of the newly launched Nature Parkinson's Journal. . Professor K Ray Chaudhuri has particular expertise in non-motor aspects of PD focused on subtyping, sleep and pain.



IORELLA CONTARINO

/The Netherlands

M. Fiorella Contarino received her MD cum laude from the Università Cattolica del Sacro Cuore, in Rome, Italy, in 2000 with a dissertation entitled “Deep brain stimulation for the treatment of Parkinson’s disease”. In 2005 she obtained the degree of Neurologist at the same University.

She then moved to The Netherlands and started working at the Academic Medical Centre (AMC) in Amsterdam, where she was appointed as researcher until 2016. In 2013 she received the PhD in Neuroscience at the University of Amsterdam, The Netherlands, with a dissertation entitled “DBS for movement disorders: toward an improvement of surgical treatment”.

Since 2012 she is working as clinical neurologist at the Haga Teaching Hospital in The Hague, The Netherlands and since 2016 she is also appointed as researcher at the Leiden University Medical Centre (LUMC), The Netherlands, combining clinical work and research in the field of movement disorders.

Her main field of interest is the study of movement disorders, with a focus on neurostimulation approaches. She has been involved as co-investigator and principal investigator in clinical trials concerning deep brain stimulation for Parkinson’s disease, dystonia, and tremor, and the development of new technologies in the field of stereotactic surgery.

She has also been involved in studies on new clinical applications of Botulinum toxin and development of new medications in the field of movement disorders.

Furthermore, she contributed to the clinical characterization of patients with familial forms of dystonic syndromes and parkinsonism in the context of genetic studies.

In 2010 she was awarded the “Hans Speelman prize” on behalf of the Dutch Society for Functional Neurosurgery for Movement Disorders (NVFNB) for work in the field of DBS.

She is regularly involved in national and international teaching activities on the topic of Movement Disorders and is responsible of an international DBS training in the DBS center of Haga Teaching Hospital/LUMC (YNLTP - Young Neurologists’ Training Program).

She has published 64 papers in peer-reviewed journals, and has an H-index of 21.

She has been Guest Editor for the Research topic: “Diagnostic issues in Hyperkinetic disorders” for the journal *Frontiers in Neurology* - specialty session “Movement Disorders”, and is member of the review editorial board of *Parkinsonism and Related Disorders*, *Frontiers in Neurology* - specialty session “Movement Disorders”, and *Frontiers in Psychiatry* - specialty session “Neuropsychiatric Imaging and Stimulation”.



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CRISTIAN FALUP-PECURARIU

/Romania

Cristian Falup-Pecurariu is Head of the Department of Neurology, County Emergency Clinic Hospital from Brasov, and is Lecturer of Neurology at the Transilvania University from Braşov, Romania. He received his medical degree from the University of Medicine and Pharmacy "Iuliu Haţieganu" from Cluj-Napoca.

He hold a 1 year fellowship of the European Neurological Society in movement disorders and sleep medicine at Hospital Clinic, University of Barcelona, Spain.

During his career Cristian Falup-Pecurariu was President of the European Association of Young Neurologists and Trainees (EAYNT), EAYNT Liasion Officer with World Federation of Neurological Society, co-representative of Europe on the International Working Group for Young Neurologists and Trainees (World Federation of Neurology). He was also Secretary of the EFNS/MDS-ES Panel on Movement Disorders, member of the Educational Committee of MDS-ES and currently is member of the MDS Leadership Task Force and European Academy of Neurology Scientific Panel Movement Disorders. He is member of EUROPAR (European Parkinson's Group) and International Parkinson and Movement Disorders Society Non motor study group.

He is the founder and Course Director of the Movement Disorders Teaching Course held in Brasov.

His research focuses on non-motor aspects of Parkinson's diseases and restless legs syndrome.



SHARON HASSIN-BAER

/Israel

Prof. Sharon Hassin-Baer received her medical degree from the University of Tel-Aviv, Sackler Faculty of Medicine, and completed her residency in Neurology at Sheba Medical Center, Tel Hashomer, Israel. She then trained in Movement Disorders with Professor Nir Giladi at Tel-Aviv Sourasky Medical Center, following which she returned to Sheba and opened the Parkinson's disease and Movement disorders clinic. In January 2014 the clinic had turned into an institute and she was nominated to direct it.

Prof. Hassin-Baer is a clinician and researcher whose practice and research focus on Parkinson's disease and other movement disorders, including ataxia, tremor, as well as on other rare neurogenetic disorders. She is also a leading figure in advanced therapies, notably functional stereotactic interventions for movement disorders in Israel.

Prof. Hassin-Baer is a member of the Movement Disorder Society (in which she is a member of the Membership and Public Relations Committee) and of the Israeli Neurological association (in which she is a member of the scientific committee and the head of the health basket committee). Prof. Hassin-Baer is strongly associated with the Israel Parkinson Association for which she serves as head of the medical advisory board.

Prof. Hassin-Baer has authored or co-authored over 60 articles, abstracts, book chapters and other materials on Parkinson's disease, deep brain stimulation, genetics of movement disorders and related issues, and has lectured widely on these topics all over Israel. She and her staff have presented the research findings in scientific meetings around the world. Her articles have been published in leading medical research journals in the field of neurology, including the Movement Disorders journal, Parkinsonism and Related Disorders, JAMA Neurology, Neurogenetics, Journal of Neurology, Neurology, Annals of Neurology and more.

Throughout her career Prof. Hassin-Baer has held many teaching positions, beginning during her residence years in Nursing school, and ever since her specialization in Tel-Aviv University Medical School and school of physiotherapy in which she heads both undergraduate Neurology course and Movement Disorders Masters course.

Prof. Hassin-Baer has been a principal investigator in several international studies of treatments for Parkinson's disease and other Movement Disorders.

Her research has been supported by the generous donations of the The Bharier Medical Fund, Gonda Foundation, the Saia Foundation (Tel-Aviv University), the Ministry of Science and industry and by the Office of the chief Scientist (OCS) at the Ministry of the economy, Israel.



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PETER JENNER
/UK

Prof Peter Jenner Peter is a world-renowned specialist in preclinical aspects of Parkinson's and other neurodegenerative diseases. He has expertise in drug metabolism and pharmacokinetics but neuropharmacology based on functional models of neurodegenerative diseases has formed the major focus of his work. Following 14 years as Head of Pharmacology, Peter is now Emeritus Professor of Pharmacology at King's College London, and a Fellow of the Royal Pharmaceutical Society, the British Pharmacological Society, the Royal Society of Medicine and of King's College London. He has published more than 700 peer reviewed papers along with many chapters and monographs. Aside from his illustrious academic achievements, Professor Jenner also has considerable industrial experience, being a Founder, Director and CSO of Proximagen, is currently CSO of Chronos Therapeutics and consults for a number of pharmaceutical companies, including USB, Teva and Lundbeck.

Professor Peter Jenner Currently Emeritus Professor of Pharmacology at King's College London, Peter is a world-renowned specialist in preclinical aspects of Parkinson's and other neurodegenerative diseases. He was previously a founder and CSO of the biotech Proximagen and is also currently CSO of Chronos



MEIKE KASTEN
/Germany

POSITION/TITLE Associate Professor in Neuropsychiatric Epidemiology

EDUCATION:

1996-2002	Medical School at the Ruhr University Bochum
1998-2002	Doctoral thesis at the Department of Psychiatry and Psychotherapy, Johannes Gutenberg Universität Mainz, Topic: Examination of Body Mass Index and leptin in patients with Narcolepsy
2002-2004 Holstein,	Neurology residency at the Department of Neurology, University Clinic of Schleswig-Campus Luebeck including 6 months protected research time
2006-2011 of	Psychiatry residency at the Department of Psychiatry and Psychotherapy, University Clinic Schleswig-Holstein, Campus Luebeck including 6 months protected research time
March 2011	Completion of Clinical Training and Board Examination for Psychiatry and Psychotherapy
January 2012	Submission of the Habilitation thesis; University of Lübeck, Medical Faculty "Non-motor symptoms in Parkinson disease"
July 2013	Associate Professor in Neuropsychiatric Epidemiology at the University of Lübeck

SCIENTIFIC TRAINING

2002-2004	Clinical research experience in the Neurogenetics group of Prof. Klein at the University of Lübeck
2004-2006	Neuroepidemiology Fellowship (Postdoctoral position) at the Parkinson's Institute in Sunnyvale, California, USA
July 2004	Movement Disorders course in Aspen, Colorado (Faculty: Prof. S. Fahn, Prof. J. Jankovic, Prof. M. Hallett)
„Summer class“ 2004 Summer quarter 2004	University of California San Francisco (UCSF); „Designing clinical research“ "Introduction to statistics" (HRP 259) at Stanford University, Department of Public Health and Epidemiology
Winter quarter 2004-2005 Summer quarter 2005	"Categorical data analysis" (HRP 261) at Stanford University "Scientific Writing" at Stanford University
June 2010	Start of the first independent research project funded by the German Research Foundation

RESEARCH FOCUS

Epidemiology of psychiatric symptoms and disorders in movement disorders



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DAFIN F. MUREȘANU
/Romania

Professor of Neurology, Senior Neurologist, Chairman of the Neurosciences Department, Faculty of Medicine, University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca, President of the Romanian Society of Neurology, President of the Society for the Study of Neuroprotection and Neuroplasticity (SSNN), member of the Academy of Medical Sciences, Romania, secretary of its Cluj Branch. He is also member of 13 scientific international societies (being member of the American Neurological Association (ANA) - Fellow of ANA (FANA) since 2012) and 7 national ones, being part of the executive board of most of these societies. Professor Dăfin F. Mureșanu is a specialist in Leadership and Management of Research and Health Care Systems (specialization in Management and Leadership, Arthur Anderson Institute, Illinois, USA, 1998 and several international courses and training stages in Neurology, research, management and leadership). Professor Dăfin F. Mureșanu is coordinator in international educational programs of European Master (i.e. European Master in Stroke Medicine, University of Krems), organizer and co-organizer of many educational projects: European and international schools and courses (International School of Neurology, European Stroke Organisation summer School, Danubian Neurological Society Teaching Courses, Seminars - Department of Neurosciences, European Teaching Courses on Neurorehabilitation) and scientific events: congresses, conferences, symposia (International Congresses of the Society for the Study of Neuroprotection and Neuroplasticity (SSNN), International Association of Neurorestoratology (IANR) & Global College for Neuroprotection and Neuroregeneration (GCNN) Conferences, Vascular Dementia Congresses (VaD), World Congresses on Controversies in Neurology (CONy), Danube Society Neurology Congresses, World Academy for Multidisciplinary Neurotraumatology (AMN) Congresses, Congresses of European Society for Clinical Neuropharmacology, European Congresses of Neurorehabilitation). His activity includes involvement in many national and international clinical studies and research projects, over 350 scientific participations as "invited speaker" in national and international scientific events, a significant portfolio of scientific articles (134 papers indexed on Web of Science-ISI, H-index: 15) as well as contributions in monographs and books published by prestigious international publishing houses. Prof. Dr. Dăfin F. Mureșanu has been honoured with: the Academy of Romanian Scientists, "Carol Davila Award for Medical Sciences / 2011", for the contribution to the Neurosurgery book "Tratat de Neurochirurgie" (vol.2), Editura Medicală, București, 2011; the Faculty of Medicine, University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca "Octavian Fodor Award" for the best scientific activity of the year 2010 and the 2009 Romanian Academy "Gheorghe Marinescu Award" for advanced contributions in Neuroprotection and Neuroplasticity.



PER ODIN

/Sweden/Germany

Professor Odin finished medical school at the Uppsala University, Sweden 1982, then presented his PhD thesis at the same university in 1987. He became specialist in Neurology 1993 at the Lund University, Sweden and got his first Professorship at the Medical School Hannover, Germany in 1998. Odin is now head of the department of Neurology at the Central Hospital in Bremerhaven, Germany and at the same time has a Professorship in Neurology at the Lund University, Sweden. Odin has focused his interest on Movement Disorders since 1987 and his main research areas concern continuous dopaminergic stimulation, pump therapies for Parkinson's disease (PD), non-motor PD symptoms and cell transplantation in PD. Odin is chair of the Scandinavian Movement Disorder Society and board member of the Competence Network Parkinson's disease in Germany. Odin is scientifically responsible for the development of the Swedish Evidence-Based Guidelines for Parkinson at the Board of Health and Welfare.



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WALTER PAULUS

/Germany

W. Paulus—studied medicine at the University of Düsseldorf and was awarded the MD with his thesis on “Psychophysics of color vision deficiency”. After specialist training in neurology in Düsseldorf and a 6-month research residence at the National Hospital for Nervous Diseases, University College London, he was in the Department of Neurology and Clinical Neurophysiology at the Alfred-Krupp Hospital and transferred then to the Neurological University Hospital at the Klinikum Grosshadern in Munich with a scientific focus on human posture regulation. In 1987 he was habilitated (German professorial qualification) in neurology and clinical neurophysiology and, in 1992, was appointed Director and chair of the Department of Clinical Neurophysiology at the University Medical Centre of the University of Göttingen. In 1997 he was the President of the German Society of Clinical Neurophysiology. He has been the coordinator of various research networks and was speaker of the international graduate school “Neuroplasticity: From Molecules to Systems”. At present he is Chairman of the European Chapter of the International Federation of Clinical Neurophysiology. In 2016 he obtained the Hans-Berger Price from the German Society for Clinical Neurophysiology for his lifework on clinical neurophysiology encompassing now some 550 publications.



LACRAMIOARA PERJU-DUMBRAVA

/Romania

Lăcrămioara Perju-Dumbravă, MD, PhD is Professor of Neurology within the Neurosciences Department, Faculty of Medicine, University of Medicine and Pharmacy “Iuliu Hatieganu” Cluj-Napoca, Chairman of the First Neurology University Clinic, Cluj-Napoca, Romania. Her academic status includes her position as member of the Board of the Faculty of Medicine and of the University’s Senate, as well as Doctorate coordinator in the field of MEDICINE. Her prestigious activity includes: publishing of 3 monographs, co-authorship in other 9 speciality books, 211 scientific papers published in medical journals, chairman and speaker at annual national congresses and conferences, international conferences and membership in editing committees and professional societies, involvement in several clinical studies, her expertise being sought by national medical councils and committees.



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MARIOS POLITIS
/UK

Marios Politis (MD MRCP MSc DIC PhD FEAN) is a Clinical Senior Lecturer, Consultant Neurologist, and the Head of Neurodegeneration Imaging Group at King's College London.

His research involves the use of molecular (PET) and functional (fMRI) imaging as a method of investigating aetiology, pathophysiology, and effects and complications of novel therapies in Neurodegenerative disorders. His high quality research has led to a body of scientific work investigating the pathophysiology of movement disorders such as Parkinson's and Huntington's disease and to publications in high impact scientific journals including Science Translation Medicine, Journal of Clinical Investigation, Brain, Neurology and JAMA Neurology. Dr Politis is a recipient of fellowships from and grant project awards from the Michael J Fox Foundation for Parkinson's research, CHDI Foundation, Medical Research Council, European Union, Lily and Edmond J. Safra Foundation, Parkinson's UK and the NIHR Biomedical Research Centre.

Dr Politis graduated in Medicine from the University of Athens, Greece, and he obtained an MSc and the Diploma of Imperial College in Integrative Neuroscience. He holds a PhD in Clinical Neuroscience from Imperial College London where he is also a Visiting Clinical Senior Lecturer in Neurology and Principal Investigator in the Neurology Imaging Unit. He has previously worked as a clinical research fellow at University College London (UCL) and Imperial College London. He is a former Research Investigator of Hammersmith's Cyclotron PET Neurology MRC CSC group, in which he received intense training for six years. He has industry experience by serving as a clinical imaging investigator for several PET Imaging trials.

He has achieved a high number of awards and distinctions including the Award for Outstanding and Innovative Clinical Research during the 16th International Congress of Parkinson's Disease and Movement Disorders in Dublin. In 2010, his PET imaging work in transplantation of foetal ventral mesencephalic tissue in Parkinson's Disease patients was classed as one of the most important research achievements of MRC-funded research. He has received for four years in a row (2013-2016) the IMPETus award for innovative and outstanding PET molecular imaging research, and in 2015 he received the PET Investigator Award from the Society of Nuclear Medicine and Molecular Imaging in Baltimore, USA. In 2016, he was elected as Fellow of the European Academy of Neurology for outstanding contribution in neurodegenerative research.

Dr Politis is a scientific advisor to the French National Research Agency (ANR), MRC, EU FP7, Canada Foundation for Innovation, Israel Science Foundation, Swiss National Science Foundation, National Research Foundation (NRF) in Korea, Austrian Science Fund, Geneva University Hospitals Research Fund, and a scientific advisory board member of the Network of European CNS Transplantation and Restoration (NECTAR), and member of European Parkinson's transplantation trial development group (TRANSEURO). He is an active member of American Academy of Neurology, Movement Disorder Society, British Neuroscience Association, and a Fellow of Royal Society of Medicine.



MATEJ SKORWANEK

/Slovakia

Matej Skorvanek is currently working as a consultant neurologist and head of the Movement Disorders Unit at the Dept. Of Neurology, Safarik University and University of L. Pasteur in Kosice, Slovakia. He was awarded a PhD in medical sciences at the University of Groningen, Netherlands on the topic of „Fatigue, apathy and quality of life in patients with Parkinson’s disease“. During his movement disorders training he spent time also at the Charles University in Prague, Czech republic and at the University College London, Queens square, London, UK. He is a 2015 awardee of the MDS International Leaders Program for Young Movement Disorder Neurologists, with prof. Kailash Bhatia as personal mentor and currently serves on a couple of MDS committees and task forces including the European Education Committee, Task Force on Rating Scales Development, Web Editorial Board, Social Media Subcommittee and Task Force on MDS-UPDRS development. His major research interests include a) clinical and tissue biomarkers of premotor PD; b) neuropsychiatric symptoms of PD with special focus on fatigue and apathy; c) non-motor symptoms in PD patients treated with DBS and pump therapies; d) clinical and genetic studies of dystonia. He currently coordinates an MDS commissioned review on cognitive rating scales in PD and he coordinates also a large international, multicenter study of 3200 PD patients looking at different aspects of the MDS-UPDRS and its relationship to quality of life.



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FABRIZIO STOCCHI

/Italy

Fabrizio Stocchi, MD, PhD, is Professor of Neurology, Consultant in Neurology and Director of the Parkinson's disease and Movement disorders research centre and director of the drug development research centre at the University and Institute for Research and Medical Care IRCCS San Raffaele Rome. He is also Scientific advisor of the Institute for Parkinson's Disease Research in Vicenza. Professor Stocchi was awarded his MD from the University of L'Aquila and his PhD from the University of Catania.

Professor Stocchi's research activities have centred on neuropharmacology in the field of movement disorders and neurodegenerative diseases.

Professor Stocchi pioneered (along with Dr. Obeso and Tom Chase) in the 80's the concept of "continuous dopaminergic stimulation" for Parkinson's disease and started the subcutaneous and intrainestinal infusion of dopaminergic drugs. He has published many books and papers on the genetics, clinical diagnosis, characterisation and treatment of Parkinson's disease, as well as in preclinical research into the disease. He is an active member of 11 societies, including the Movement Disorders Society, the WFN society where is member of the extrapyramidal committee, the European Clinical Neuropharmacology Society and the European Federation Neurological Society.



CLAUDIA TRENKWALDER

/Germany

Claudia Trenkwalder, MD, started her clinical education in neurology and movement disorders at the University Hospital of the Ludwig-Maximilian-University in Munich in 1988 and was head of the “Movement Disorders and Sleep” research group at the Max-Planck Institute of Psychiatry in Munich from 1993-2000, before moving to the Department of Clinical Neurophysiology at the University of Goettingen. She is neurologist and Professor for Movement Disorders at University Medical Center in Goettingen, and Medical Director of Elena Klinik, the largest hospital for Parkinson and Movement Disorders in Germany, since 2003.

Her main research interests are early symptoms and therapy in Parkinson disease and movement disorders in sleep (RBD and RLS). She is currently Secretary of the International Parkinson and Movement Disorder Society, but was also Founding Member of the World Association of Sleep Medicine (WASM), and President of WASM from 2011-13.

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COURSE VENUE

HOTEL ALPIN

500001 Poiana Brasov, Brasov, Romania
<http://www.hotelalpin.ro>





Course Registration Desk

All course materials and documentation will be available at the SSNN booth. The course staff will be pleased to help you with all enquiries regarding registration, course materials and program.

Please do not hesitate to contact the staff members if there is something they can do to make your stay more enjoyable.

Registration Fees

Full course registration: 200 EUR

This fee includes:

- Course booklet
- Coffee breaks
- Two lunches
- Three dinners

Standard Registration: 100 EUR

This fee includes:

- Course booklet
- Coffee breaks
- Two lunches

Futher informations:

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doria@global-t.ro



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Participants Registration Fee Includes:

Admission to all scientific sessions during the course.
Course materials (delegate bag, final program and abstract book etc.)
Admission to Lunches and Coffee Breaks

On-Site Registration

On-site registration will be processed on a first-come, first-served basis. Priority will be given to pre-registered delegates.
Depending on the number of on-site registered delegates, availability of course bags may be limited.

Name Badges

Participants are kindly requested to wear their name badge at all times during the course.
The badge allows admission to the scientific sessions, coffee breaks and lunches.

Course Language

The course language is English.
Simultaneous translation will not be provided.

Changes In Program

The organizers cannot assume liability for any changes in the course program due to external or unforeseen circumstances.



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