INTERNATIONAL PARKINSON AND MOVEMENT DISORDER SOCIETY

SOCIETY OF NEUROLOGISTS OF THE REPUBLIC OF MOLDOVA

2nd Teaching Course in Movement Disorders

Republic of Moldova
Radisson Blu Convention Center
April 11-12, 2019

ENDORSED BY THE:

INTERNATIONAL PARKINSON AND
MOVEMENT DISORDER SOCIETY

SUPPORTED BY THE:

SOCIETY OF NEUROLOGISTS OF
THE REPUBLIC OF MOLDOVA

NICOLAE TESTEMITANU
STATE UNIVERSITY OF MEDICINE
AND PHARMACY, CHISINAU,
REPUBLIC OF MOLDOVA

DIOMID GHERMAN
INSTITUTE OF NEUROLOGY AND
NEUROSURGERY, CHISINAU,
REPUBLIC OF MOLDOVA

WELCOME WORDS

DEAR COLLEAGUES AND FRIENDS!

It is our utmost pleasure to welcome you for **2nd Teaching Course in Movement Disorders** in Chisinau, Republic of Moldova – scientific event endorsed by the **International Parkinson and Movement Disorders Society.**

The course is open to all professionals interested in movement disorders diagnosis and treatment. The event is focused on Parkinsonism, hyperkinetic disorders and complex issues in movement disorders – a unique opportunity for young and experienced neurologists to receive in depth presentations from internationally-recognized Movement Disorders experts. As participants, you'll have the opportunity to attend lectures and panel discussions, as well as video case presentation sessions.

You will have the chance to engage in active discussions and enjoy cutting-edge lectures by the world's top scientists and neurologists.

The Organizing Committee wishes you to have interesting and interactive participation for all presented topics with maximum benefit for your clinical practice.

COURSE DIRECTOR

LISNIC VITALIE

- The President of the Society of Neurologists of the Republic of Moldova.
- Professor of Neurology, Department of Neurology nr. 1, Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova.
- Consultant professor, Neuromuscular Diseases Department, Institute of Neurology and Neurosurgery, Chisinau, Republic of Moldova.
- Member of the Education Committee of the World Federation of Neurology.
- Delegate of the Republic of Moldova, European Academy of Neurology.

CHAIR SCIENTIFIC COMMITTEE

MIHAIL GAVRILIUC

- Professor of Neurology, Head of the Department of Neurology nr.1, Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova.
- Consultant professor, Neuroemergencies and Stroke Department, Institute of Neurology and Neurosurgery, Chisinau, Republic of Moldova.
- Vice-rector for International Students at Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova.

FACULTY

(IN ALPHABETICAL ORDER)

- Carlo **COLOSIMO** (Terni, **Italy**)
- Cristian **FALUP-PECURARIU** (Brasov, ***Romania***)
- Mihail **GAVRILIUC** (Chisinau, ***Republic of Moldova***)
- Vitalie **LISNIC** (Chisinau, ***Republic of Moldova***)
- Ion **MOLDOVANU** (Chisinau, ***Republic of Moldova)***
- Pille **TABA** (Tartu, ***Estonia***)
- Claudia **TRENKWALDER** (Goettingen, ***Germany***)
- Stanislav **GROPPA** (Chisinau, ***Republic of Moldova***)

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- Elena COSTRU-TASNIC
- Alexandru GASNAS
- Pavel GAVRILIUC
- Evelina GHERGHELEGIU
- Elena MANOLE
- Lilia ROTARU
- Marina SANGHELI
- Victoria SIMON

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ABSTRACTS

AUTONOMIC DYSFUNCTIONS IN PARKINSON'S DISEASE

CARLO COLOSIMO
Department of Neurological Sciences, Santa Maria University Hospital, Terni, Italy

Dysautonomia is an important non-motor symptom in α-synucleinopathies, almost always present in multiple system atrophy (MSA), affecting more than 50% of patients suffering from Parkinson's disease (PD) and Lewy body dementia (LBD). In my presentation I will initially focus on the clinical feature and management of cardiovascular dysautonomia associated with PD. In addition, I will discuss how several epidemiological studies have highlighted the negative prognostic effect of cardiovascular dysautonomia on cardiovascular and cerebrovascular outcomes as well as on overall mortality in all α-synucleinopathies. Altered cerebral perfusion, vascular pressure stress, and related disturbance of the blood-brain barrier may contribute to the frequently occurring white matter changes and cognitive dysfunction in patients affected by neurovascular instability. I will finally review the current knowledge on the pathophysiology of cardiovascular dysautonomia and its impact on disease outcome and cognitive functions in α-synucleinopathies, supporting the theory that cardiovascular dysautonomia, although not being a primary cause of disease, may significantly affect disease progression and therefore requires careful screening and best available clinical management.

COGNITIVE DYSFUNCTION AND DEMENTIA IN PARKINSON'S DISEASE

CARLO COLOSIMO
Department of Neurological Sciences, Santa Maria University Hospital, Terni, Italy

Subtle cognitive dysfunction is common in Parkinson's disease (PD) since its early phases, and eventually up to 40-70% of parkinsonian patients will develop full-blown dementia. My presentation will be mainly focus on the diagnosis of dementia associated with PD. During the routine use of the most commonly used sets of criteria for this disease (UK PD Society Brain Bank criteria, UKPDSBB) spanning now for more than two decades, most researchers and clinicians have found several significant limitations. First, these criteria focus only on motor features whereas it is now widely accepted that PD is associated with numerous non-motor features more or less responsive to levodopa, including sleep disturbances, mood disorders, autonomic failure, sensory problems, and cognitive impairment. In particular, cognitive impairment is common in PD but, according to the UKPDSBB criteria, it might challenge a clinical diagnosis of PD if severe enough to configure dementia within the first year of motor symptom onset. In this case, cognitive impairment would become an exclusion criterion for PD leading to an alternative diagnosis of DLB. However, the reciprocally exclusive relationship between PD-dementia and DLB has remained quite controversial, since both disorders present with parkinsonism and dementia, and both are Lewy body disorders and synucleinopathies, leading several experts to think that they should be considered on a spectrum of the same disorder. This consideration has been fully received by the more recent MDS criteria for diagnosis of PD released in 2015.

TREMOR

CARLO COLOSIMO
Department of Neurological Sciences, Santa Maria University Hospital, Terni, Italy

Tremor is defined as rhythmic, oscillatory involuntary movement. It is a common symptom of a several neurological disorders, and a disease entity in itself. The diagnostic process of patients with tremor can be time-consuming and difficult, and an effective treatment fails or is postponed due to limited diagnostic instruments. Even if treatment is successful, the therapeutic process could take a long period, involving various drugs, with the consequence of frequent side-effects of medication. This process can also be costly, since wrong diagnostic tests and wrong types of drugs may be used (common examples will be given). The objective of my presentation is to provide a practical clinical guideline with respect to diagnosing tremor disorders. Different types of tremor, including common and unusual forms, their clinical features and underlying pathophysiology will be presented. The diagnostic use of ancillary examinations in the light of differentiating tremor syndromes will be also discussed. Finally, I will propose a flow chart on how to therapeutically approach patients presenting with different causes of tremor.

EXAMINATION OF PARKINSON PATIENTS: A TRAINING SESSION

CRISTIAN FALUP-PECURARIU
Department of Neurology, Faculty of Medicine, Transilvania University, County Emergency Clinic Hospital, Brasov, Romania

Parkinson's disease (PD) is a complex neurodegenerative disorder. The most well-known features of PD are the motor ones: bradykinesia, rest tremor, extrapyramidal rigidity and postural instability. Beside the motor signs, patients with PD might present with a great variety of non-motor symptoms, including mood disturbances, sleep disorders, gastrointestinal symptoms, impairment of cognitive function, autonomic dysregulation, etc.

With the exception of few imagistic studies that are able to certify the alteration of the nigro-striatal pathway, the diagnosis of PD is entirely clinic. In addition to this, the severity of PD is also graded using the physician's clinical skills.

The most widely used tools that are helpful in assessing the motor clinical manifestations and the severity of PD are the UPDRS and UDysRS rating scales.

In 2001, the Movement Disorder Society (MDS) sponsored a revision of the UPDRS. Hence MDS-sponsored UPDRS revision (MDS-UPDRS) was launched by MDS. This new version provides more details and instructions and solves some ambiguities from the original version.

MDS-UPDRS (Unified Parkinson's Disease Rating Scale) comprises four parts that evaluate the non-motor and motor aspects of daily living, the motor clinical examination and the motor complications of PD. UDysRS

(Unified Dyskinesia Rating Scale) was developed to assess dyskinesia and dystonia, which are among the most frequent motor complications of the antiparkinsonian treatment. It has four parts and it is designed to be filled out by both the patient (and caregiver) and the rater.

The aim of this training session is to offer a practical perspective of the clinical examination of PD patients, focusing on key-points of using the MDS-UPDRS and UDysRS scales.

This will be an interactive session that will show the key elements of the MDS-UPDRS. There will be case series that would allow participants to better understand the application of these rating scales.

SLEEP DISORDERS IN PARKINSON'S DISEASE

CRISTIAN FALUP-PECURARIU

Department of Neurology, Faculty of Medicine, Transilvania University, County Emergency Clinic Hospital, Brasov, Romania

Sleep disorders are commonly encountered in Parkinson's disease (PD), being reported by more than half of the patients. These symptoms are recognized as being clinically relevant by the PD patients and may significantly affect their quality of life. Sleep disorders in PD can be classified into: disturbances of sleep and disturbances of wakefulness. All types of sleep disorders may be encountered in PD: insomnia, excessive daytime sleepiness (EDS), rapid eye movement sleep behavior disorders (RBD), restless legs syndrome and sleep-disordered breathing. Insomnia in PD patients has an estimated prevalence of 40% and it has important consequences, like sleepiness, fatigue, mood disorders. EDS is another frequent complaint among PD patients and it is characterized by difficulties in staying awake in passive or active situations. Episodes of sudden onset of sleep might also occur. RBD has a prevalence of 19-70% and constitutes one of the prodromal symptoms of PD, being manifest even before the occurrence of the motor symptoms.

The etiology of sleep disorders in PD is multifactorial and it might be related with the degeneration of the sleep-regulating structures. The severity of the motor features and of other non-motor symptoms might influence the quality of sleep. The assessment of the sleep disorders can be done with generic and specific scales, but also using sleep recording techniques, like actigraphy or polysomnography. This lecture will focus on reviewing the classification, definition and the characteristics of the most frequent sleep disturbances encountered in PD, along with their pathophysiology, assessment, and management.

TICS AND GILLES DE LA TOURETTE'S SYNDROME

MIHAIL GAVRILIUC
Head of Department of Neurology nr.1, Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

Tics and Gilles de la Tourette syndrome remain a challenge in terms of diagnosis and treatment difficulties. Although they do not have vital disorders, childhood onset of these movement disorders category is a disturbing subject for parents, educators and teachers. But also most family doctors, pediatricians, neurologists and psychiatrists are not much enthusiastic when they are involved in monitoring and treating this patient population.

The classification in primary (idiopathic) and secondary (symptomatic) ticks allows from the beginning to separate those whose pathogenicity is clear from those whose mechanisms of occurrence to date are not fully known (primary) and are the subject of clinical research and fundamental underway. Simple primary childhood tics as well as any other movement disorders require to be properly diagnosed, but finally, however, it is solved by itself without any medication. In some cases, they persist in the adult life, but can be easily masked or detained voluntarily or interpreted as "mannerism." A more serious problem in this regard is Gilles de la Tourette syndrome because it includes multiple tics, vocalizations, as well as psychiatric comorbidities, which causes restrictions and social / professional barriers for patients.

The correct attitude of family members, staff of educational institutions, evaluation of obsessive-compulsive behavior, as well as the correct choice of medication (including deep brain stimulation) today make it possible to substantially improve the quality of patients' lives.

AVAILABLE TREATMENT OPTIONS FOR PD PATIENTS IN THE REPUBLIC OF MOLDOVA

VITALIE LISNIC
Department of Neurology nr.1, Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

The diagnosis of Parkinson's disease (PD) was established at 2400 patients at the Institute of Neurology and Neurosurgery in Chisinau, Republic of Moldova (RM). The active treatment of PD begins at the time of diagnosis. Early treatment with dopaminergic therapies is recommended, and the choice is between levodopa preparations, dopamine agonists, and monoamine oxidase inhibitors (MAO).

In younger patients are still used anticholinergics (Trihexyphenidil in daily dosage up to 6-8 mg). MAO inhibitors and dopamine agonists are longer-acting medications and therefore require only one dose per day. From MAO inhibitors available in RM is only Selegiline which is given in a dosage of 5-10 mg per day. As dopamine agonists are used Pramipexole (tablets of 0,18 and 0,7 mg) in daily dosage up to 3,0-4,5 mg and Ropinerole (tablets of 1 and 2 mg) in daily dosage 4-24 mg. Extended release forms are not available yet. Levodopa, in combination with a dopa decarboxylase inhibitor (Levodopa/Carbidopa and Levodopa/Benserazide), is more efficacious but requires dosing intervals of 3 times per day initially. COMT inhibitors (entacapone and tolcapone) are not yet available in RM.

The dose adjustments of dopamine agonists and levodopa preparations are made in response to clinical effect, emerging symptoms, and side effects. The gold rule is to try to treat with the lowest dose possible to achieve benefits and reduce adverse reactions. The risk of psychiatric

side effects and dyskinesias is greater at higher doses. Patients below 50 years of age who take doses of greater than 600 mg of levodopa are more likely to experience dyskinesia.

As the disease progresses, motor fluctuations with end-of-dose wearing off symptoms or peak-dose dyskinesias are inevitable. Initially, the fluctuations will respond well to medication manipulation. Wearing-off symptoms can be alleviated by the addition of dopamine agonists, or with increased levodopa dosing frequency. Dyskinesias develop in about 50% of patients with PD, including patients treated with dopamine agonists, levodopa preparations, or MAO inhibitors. They are more likely to develop in patients using higher doses of levodopa preparations, in men, and in younger patients. Often, when mild, they do not need any specific treatment. Where possible, doses of dopaminergic medications should be minimized, and in some patients the addition of amantadine can reduce the dyskinesias.

Treatment of depression, anxiety, insomnia will often require the addition of tricyclic antidepressants (Amitriptyline, Imipramine), selective serotonin reuptake inhibitors (Escitalopram, Sertraline, Fluvoxamine, Paroxetine, Fluoxetine) or serotonin-norepinephrine reuptake inhibitors (Duloxetine, Venlafaxine).

FUNCTIONAL MOVEMENT DISORDERS: TOWARDS TO IDENTIFYING THE UNION BETWEEN THE MIND AND BODY

ION MOLDOVANU

Institute of Neurology and Neurosurgery, Department of Neurology nr.1, Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

Functional movement disorders (FMD) are considered to be those induced by psychological causes, although, in fact, complete patho-physiology is not fully known. Patients with FMD are commonly found in neurological practice and may be incapacitated and cause significant discomfort. The new DSM-5 criteria for the FMD no longer require the presence of a "psychological conflict", suggesting that some patients with FMD have no obvious psychological comorbidity. Despite the fact that the diagnostic criteria for most of the functional neurological movement disorders are being developed, diagnosis remains a difficult one, often posing a real challenge.

Neuroimaging studies, especially functional magnetic resonance imaging, have shown that FMD are involuntary. The study of resting-state functional connectivity has highlighted the presence of specific connections that could be used as biomarkers with high diagnostic value in future clinical practice to identify individual FMD patients (Wegrzyk J. et al., 2018). The data provided by neuroimaging investigations can not yet elucidate the ethyologic and pathogenetic aspects of FMD (Kranick S. et al., 2011).

Functional movement disorders continue to represent a "crisis for neurology" (Hallet M, 2006) or express a "linguistic crisis" (Hagger MS, Orbell

S., 2003). It is necessary to defeat Cartesian dualism that has dominated centuries in the West, the unity between mind and body is required to be identified and founded (Dallocchio C. et al., 2015). This presentation will focus on the prospects of overcoming separation and creating an integrated vision of mind-body unity, a vision that could unravel the enigma of functional movement disorders.

EPIDEMIOLOGY OF PARKINSON'S DISEASE: PROVIDING WITH PROGNOSTIC CLUES?

PILLE TABA
Head of Department of Neurology and Neurosurgery
University of Tartu, Estonia

Though discoveries on molecular pathogenesis of Parkinson's disease (PD) have changed our understanding of determinants of the disease, the etiology PD has remained obscure. Epidemiologic studies have confirmed aging as the most important component in the pathogenesis of PD, but also provided the evidence on a key role of environmental and behavioural factors in development and progression of the disease. Thus the risk for PD is multifactorial, resulting from complicated interaction between environmental, genetic and epigenetic factors affecting numerous fundamental cellular processes. Though genetic studies have revealed several monogenic mutations associated with PD, 90% of cases have no identifiable genetic cause. However, whole-genome association studies have identified a growing number of disease-predisposing genes. From other side, environmental factors with neuroprotective or neurotoxic properties may alter the risk for development and progression of PD, that is a key issue of epidemiologic studies on prevalence, incidence and mortality of PD. Clinical, radiologic and laboratory markers in large epidemiologic cohorts, especially in repeated studies, are of high value in finding the factors having an impact on the disease progression, and availabilities to modify the course of the disease. Repeated epidemiologic studies of PD showing an increasing prevalence, demonstrate ongoing growing burden of PD upon society, in the view of continuously aging populations.

TREATMENT OF ADVANCED PARKINSON'S DISEASE

PILLE TABA
Head of Department of Neurology and Neurosurgery
University of Tartu, Estonia

Progressive disability from Parkinson disease (PD) is driven by the combination of cardinal motor features, the development of levodopa-induced motor complications, and non-motor problems with increasing severity. Though levodopa is still the most effective antiparkinsonian medication, it becomes less effective as the disease progresses, and levodopa treatment-related motor and non-motor fluctuations and dyskinesias emerge in majority of patients. The main risk factors for the development of motor complications are higher cumulative dose of levodopa, longer treatment duration of levodopa, and longer disease duration. Treatment strategies aiming at less pulsatile dopaminergic stimulation are of benefit: the use of smaller and more frequent doses of levodopa, and adding MAO-B inhibitors and COMT-inhibitors. Dyskinesias may improve with levodopa dose reduction, and amantadine treatment. Device-aided interventions should be considered for controlling motor complications, or if motor symptoms do not respond sufficiently to oral treatments: subcutaneous apomorphine infusion, continuous jejunal infusion of levodopa-carbidopa intestinal gel, and deep brain stimulation (DBS). It is important to treat each patient individually, focussing on which motor as well as non-motor symptoms that are most bothersome to the patient. Team based multidisciplinar management is of high importance, including physiotherapy, speech therapy, social and practical support, collaborating with a patient and family by personalised approach.

SECONDARY MOVEMENT DISORDERS: PHENOMENOLOGY AND MANAGEMENT

PILLE TABA
Head of Department of Neurology and Neurosurgery
University of Tartu, Estonia

Secondary movement disorders include variable hypokinetic and hyperkinetic syndromes of a range etiology, including a list of medications and illicit drugs, metals, organic solvents, pesticides, methanol and other toxins, and also vascular and immunological causes, among them systemic diseases, infections, paraneoplastic syndromes and autoimmune encephalitis. Secondary movement disorders often manifest as complex syndromes including symmetrical parkinsonism with gait disorders and falls but without the resting tremor, and are combined with variable hyperkinetic features like myoclonus or dystonias, accompanied by neuropsychiatric disturbancies, prominently cognitive decline and behavioural disorders. Diagnosis of secondary movement disorders is challenging, and several radiologic and laboratory investigations might be needed, considering variable etiologies. For possibly effective management, early recognition and correct diagnosis are critical for relevant therapeutic interventions, though treatment options might suboptimal.

EARLY SYMPTOMS IN PARKINSON'S DISEASE – DIAGNOSIS AND TREATMENT; NEWS FROM RESEARCH STUDIES

CLAUDIA TRENKWALDER

Professor of Neurology and Movement Disorders, Medical Director of Paracelsus-Elena Hospital, Kassel, Germany

The diagnosis of Parkinson's disease (PD) continues to be established only by the presence of the cardinal motor features: hypokinesia, tremor and rigidity (2 out of 3), according to UK Brain Bank Criteria. Recently, our knowledge about both, the variety of motor symptoms in PD, and non-motor features has increased, but we still don't know, how these symptoms develop over time. Currently, it seems that motor symptoms are not the first but the last symptoms to emerge. The apparition of the first signs in the gastrointestinal system, in sleep-wake regulation and in the autonomic nervous system precede motor symptoms by many years. When motor symptoms start, more than 50% of dopaminergic neurons in the substantia nigra are already degenerated, and long before the affection of these midbrain areas α-synuclein positive pathology occurs in the lower brainstem, the autonomic nervous system and olfactory bulb. This peripheral origin of PD has recently been confirmed i.e. by SPECT studies investigating the gastrointestinal autonomic nervous system. Clinically, the following symptoms can variably occur in the early phase of PD: (1) Impaired olfaction, (2) autonomic disturbances i.e.constipation and orthostatic hypotension, (3) cognitive alterations such as slow reaction time and impaired executive function, (4) sleep disorders such as excessive daytime sleepiness, insomnia and most specifically REM-sleep behavior disorder (RBD).

These observations were made years ago in clinical cohorts that developed idiopathic RBD, and now, with a more than 18-year follow-up more than 80% of the subjects of the cohort have developed a neurodegenerative disease. But even subtle motor features may precede the cardinal motor signs of PD. Despite controversial discussions in the literature, some publications report an increased prevalence of postural tremor preceding rest tremor in early PD by many years. Although many of the above described features can be part of a premotor parkinson phase, unfortunatley none of these parameters could be shown in each single PD patient, some PD patients even miss many of these non-motor features or develop them later in the disease. Therefore the variation of the non-motor and motor phenotype in early PD may reflect the different pathways.

Early treatment of PD still includes levodopa/carbidopa as first line therapy, in patients younger than 65 years, and when available, dopamine agonist and/or MAO-B inhibitors such as selegeline or rasagiline, which may precede levodopa or be combined with it. New treatment trials have started a strategy using alpha synucleine antibody therapy as possible disease modifying treatment. Trials are currently ongoing, results can be expected in about 1-2 years.

DIFFERENTIAL DIAGNOSIS OF PARKINSON SYNDROMES: ATYPICAL PS, SYMPTOMS AND VIDEOS

CLAUDIA TRENKWALDER
Professor of Neurology and Movement Disorders, Medical Director of Paracelsus-Elena Hospital, Kassel, Germany

The four major differential diagnosis of idiopathic Parkinson Disease are Progressive Supranuclear Palsy (PSP), Multiple Syste Atrophy (MSA) and Cortico-Basal Degenerative Syndrome (CBD) and Dementia with Lewy Bodies (DLB).

Neuropathologically, PSP and CBD are tauopathies, MSA and DLB are synucleinopathies such as PD.

All these neurodegenerative diseases are characterized by Parkinson syndromes, but show additional features, often called "red flags", which indicate the development of an atypical parkinson syndrome and show less or no response to levodopa treatment.

The following publications currently define the atypical PS:

PSP:

Höglinger et al , *Mov Disord 2017* „The authors identified four functional domains (ocular motor dysfunction, postural instability, akinesia, and cognitive dysfunction) as clinical predictors of PSP. Within each of these domains, they propose three clinical features that contribute different levels of diagnostic certainty: probable PSP, possible PSP, and suggestive of PSP. Clinical clues and imaging findings represent supportive features."

CBD:

Armstrong et al, Neurology 2013: „Consensus Criteria: 4 CBD phenotypes emerged: corticobasal syndrome (CBS), frontal behavioral-spatial syndrome (FBS), nonfluent/agrammatic variant of primary progressive aphasia (naPPA), and progressive supranuclear palsy syndrome (PSPS). Clinical features of CBD cases were extracted from descriptions of 209 brain bank and published patients, providing a comprehensive description of CBD and correcting common misconceptions. Clinical CBD phenotypes and features were combined to create 2 sets of criteria: ... probable CBD and broader criteria for possible CBD ...“

MSA:

Gilman et al, Neurology 2008: MSA is typically characterized by parkinsonism, autonomic dysfunction, and a combination of cerebellar and pyramidal signs. MSA is classified according to the predominant phenotype at onset into MSA-parkinsonism (MSA-P) or MSA-cerebellar type (MSA-C), and up to 80% of the patients develop most of the characteristic features during the course of the disease.

“The new criteria retain the designations of definite, probable, and possible MSA. Definite MSA requires neuropathologic demonstration of CNS alpha-synuclein–positive glial cytoplasmic inclusions with neurodegenerative changes in striatonigral or olivopontocerebellar structures. Probable MSA requires a sporadic, progressive adult-onset disorder including rigorously defined autonomic failure and poorly levodopa responsive parkinsonism or cerebellar ataxia. Possible MSA requires a sporadic, progressive adult-onset disease including parkinsonism or cerebellar ataxia and at least one feature suggesting autonomic dysfunction plus one other feature that may be a clinical or a neuroimaging abnormality.”

DLB:

McKeith et al, Neurology 2017

Revised criteria for the diagnosis of probable and possible dementia with Lewy bodies (DLB)

Essential for a diagnosis of DLB is dementia, defined as a progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational functions, or with usual daily activities. Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression. Deficits on tests of attention, executive function, and visuoperceptual ability may be especially prominent and occur early.

Core clinical features (The first 3 typically occur early and may persist throughout the course.)

Fluctuating cognition with pronounced variations in attention and alertness. Recurrent visual hallucinations that are typically well formed and detailed. REM sleep behavior disorder, which may precede cognitive decline. One or more spontaneous cardinal features of parkinsonism: these are bradykinesia (defined as slowness of movement and decrement in amplitude or speed), rest tremor, or rigidity.

Supportive clinical features

Severe sensitivity to antipsychotic agents; postural instability; repeated falls; syncope or other transient episodes of unresponsiveness; severe autonomic dysfunction, e.g., constipation, orthostatic hypotension, urinary incontinence; hypersomnia; hyposmia; hallucinations in other modalities; systematized delusions; apathy, anxiety, and depression.

BIOGRAPHIES

CARLO COLOSIMO

Dysautonomia is an important non-motor symptom in α-synucleinopathies, almost always present in multiple system atrophy (MSA), affecting more than 50% of patients suffering from Parkinson's disease (PD) and Lewy body dementia (LBD). In my presentation I will initially focus on the clinical feature and management of cardiovascular dysautonomia associated with PD. In addition, I will discuss how several epidemiological studies have highlighted the negative prognostic effect of cardiovascular dysautonomia on cardiovascular and cerebrovascular outcomes as well as on overall mortality in all α-synucleinopathies. Altered cerebral perfusion, vascular pressure stress, and related disturbance of the blood-brain barrier may contribute to the frequently occurring white matter changes and cognitive dysfunction in patients affected by neurovascular instability. I will finally review the current knowledge on the pathophysiology of cardiovascular dysautonomia and its impact on disease outcome and cognitive functions in α-synucleinopathies, supporting the theory that cardiovascular dysautonomia, although not being a primary cause of disease, may significantly affect disease progression and therefore requires careful screening and best available clinical management.

CRISTIAN FALUP-PECURARIU

Cristian Falup-Pecurariu is Head of the Department of Neurology, County Emergency Clinic Hospital from Brasov, and is Associate Professor of Neurology at the Transilvania University from Brasov, Romania. He received his medical degree from the University of Medicine and Pharmacy "Iuliu Hatieganu" 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, member of the MDS Leadership Task Force and European Academy of Neurology Scientific Panel Movement Disorders. Currently he is member of the Executive Committee of MDS-European Section. Cristian Falup-Pecurariu is member of EUROPAR (European Parkinson's Group) and International Parkinson and Movement Disorders Society Non motor study group. He is the initiator 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.

MIHAIL GAVRILIUC

1987-1991 : Neurologist at the Republican Clinical Hospital, Chisinau

1991-1996 : Assistant professor of the Department of Neurology and Neurosurgery

at the State University of Medicine and Pharmacy “Nicolae Testemitanu” Chisinau

1996-2001 : Docent of the Department of Neurology and Neurosurgery at the State University of Medicine and Pharmacy “Nicolae Testemitanu” Chisinau

2001-2010 : Deputy Director of the Institute of Neurology and Neurosurgery, Chisinau

2010 (since) : Professor of Neurology, Chairman of the Neurology Department at the

State University of Medicine and Pharmacy “Nicolae Testemitanu” Chisinau

2010-2012 : Dean of the Faculty of Medicine 2 - State University of Medicine and Pharmacy “Nicolae Testemitanu” Chisinau

2012-2018 : Vice-rector for International Relations - State University of Medicine and Pharmacy “Nicolae Testemitanu” Chisinau

2018 (since) : Vice-rector for International Students - State University of Medicine and Pharmacy “Nicolae Testemitanu” Chisinau

Fields of special interests: general neurology, ischemic tolerance of the nervous system, and medical education.

VITALIE LISNIC

Professor of Neurology, responsible for postgraduate education of the residents at the State University of Medicine and Pharmacy „Nicolae Testemitanu", consultant neurologist at the Institute of Neurology and Neurosurgery in Chisinau, Republic of Moldova.

Dr. Lisnic graduated with mention the Faculty of General Medicine of the Chisinau State Medical Institute in 1989. He passed internships in Neurology and Neurophysiology in Moscow, Russian Federation, 1993; Charles University, Pilsen, Czech Republic, 1994; Landesnervenklinik of Salzburg, Austria, 1999; Emory University, Atlanta, USA, 2002 - 2003, Vienna University, Austria, 2008. In 2003 obtained a clinical attachment in neuropathies at the National Institute of Neurology, Queen's Square, London, UK.

V. Lisnic defended the thesis of doctor of science on amyotrophic lateral sclerosis (1995) and the thesis of habilitat doctor of medical science on impairment of the central nervous system in demyelinating neuropathies (2006). The main fields of clinic expertize and scientific interests are peripheral nerve disorders, neuromuscular diseases. He was the Principal Investigator in several research projects in neuropathies, postherpetic neuralgia, neuropathic pain, depressive disorders.

Vitalie Lisnic is the President of the Society of Neurologists of the Republic of Moldova, Fellow of the European Academy of Neurology. He is a member of the Education Committee of the World Federation

of Neurologists, member of American Academy of Neurology, European Stroke Organization, Movement Disorders Society, Romanian Society of Electrodiagnostic Neurophysiology.

Professor Vitalie Lisnic is the author of 2 monographs, more than 150 scientific publications in Moldovan and International biomedical journals. Under his guidance were defended 5 Ph.D theses.

ION MOLDOVANU

Ion Vasile MOLDOVANU, Republic of Moldova (RM) citizen, MD, PhD., Professor of Neurology, specialist in chronic pain (especially primary and secondary headaches), autonomic nervous system and movement disorders.

For many years professor Moldovanu develops the concept of the Functional Neurology using different models of functional and organic neurological pathologies. Currently he is concerned with the study of the phenomenon of consciousness and altered states of consciousness (in collaboration with specialists in the field of physiology, biophysics and quantum physics) in order to develop a novel therapeutic non-pharmacological approach by means of neurostimulation techniques.

Professor Ion Moldovanu is currently working in the Neurology Department of Medical and Pharmaceutical University “Nicolae Testemitanu” of the Republic of Moldova and in the Institute of Neurology and Neurosurgery as senior researcher.

Academic positions: researcher at the Neurology department of the Medical Institute “I. M. Secenov” (Moscow, Russia), Head of the Department of Neurology of Medical and Pharmaceutical University “Nicolae Testemitanu” of the Republic of Moldova (1998-2009), Director of the Institute of Neurology and Neurosurgery (2009-2013).

He founded and is actually President of the Society of Headache and Pain of the RM, vice President of Neurological Society of the RM, honorary member of the French Society of Neurology, the founder and

President of the Association of Psychoanalysis and Psychosomatic in Moldova.

International cooperation: scientifical research program in movement disorders at the Premontre Hospital (France) in connection with Salpetriere Clinic (Paris, France) – 1991-1993, visiting Professor at the University "Joseph Fourier" (Grenoble, France, 1996), at the Institute of Neuroscience from the Paris VI University (Paris, France, 1997), Fulbright clinical and scientifically research Program in the Mayo Clinic Headache Center (Scottsdale, Arizona, USA, 2002-2003), practical clinical training in the Headache Emergency Center of the Lariboisiere Hospital (Paris, France, 2006), etc.

Author of about 350 scientific papers, co-author of 2 books, 3 monographs, 1 compendium, 3 patents. He trained 17 doctors in medical science and is currently leading 6 MD thesis in progress.

PILLE TABA

Professor Pille Taba is a Head of Department of Neurology and Neurosurgery of the University of Tartu, President of the Estonian Society of Neurologists and Neurosurgeons, and Head of the Neurology Commission for the Ministry of Social Affairs. She serves as a Chair of the Education Committee of the European Section and a member of the International Executive Committee of the Movement Disorders Society, a member of the Management Groups for Panels on Movement Disorders and Infectious Diseases of the European Academy of Neurology, and a member of the Scientific Advisory Group of Neurology of the European Medicines Agency.

Pille Taba was graduated from the University of Tartu, Estonia, and received her postgraduate medical training at the University of Vienna, the University College London, the Karlstad University Hospital, and the Minneapolis Clinic of Neurology. Her research interests have been focused on movement disorders including variable aspects Parkinson's disease, toxic parkinsonism, and infections of the central nervous system. She has broad research contacts, among them collaboration with the University College London, University of Helsinki, and Uppsala University. Pille Taba has been an invited speaker at many international congresses and educational courses.

CLAUDIA TRENKWALDER

Claudia Trenkwalder, MD, started her clinical education in neurology and movement disorders at the Department Neurology of the University Hospital in Munich in 1988, 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 University Medical Center of Goettingen. Since 2003 she is Medical Director of the Paracelsus-Elena Klinik, in Kassel, and since 2012, she is Full Professor of Neurology as a Foundation Chair at Department of Neurosurgery, University Medical Center Goettingen, Germany.

She has published more than 380 peer reviewed papers and is currently President-Elect of IPMDS, and was President of WASM (World Association of Sleep Medicine) from 2011-13 and active member of many national and international scientific societies.

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