



# **The 7<sup>th</sup> Summer School of ASNER, The Romanian Society of Electrodiagnostic Neurophysiology**

**SDV2016, Eforie Nord, Romania  
8-10 July 2016**

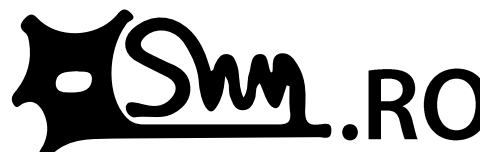
**Abstract book**



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THE SOCIETY FOR THE STUDY OF  
NEUROPROTECTION AND  
NEUROPLASTICITY



**International Federation of Clinical Neurophysiology**

Dear Friends,

It's again July, and that means it is again time for the Summer School in Clinical Neurophysiology. We are now starting this scientific event for the 7<sup>th</sup> time, so I suppose we are entitled to call it a tradition. Some of you have participated every year, many of you have attended this school a few times, and others are newcomers, but all of us have one thing in common, namely our passion for neurophysiology. We have prepared a scientific program that will contain a plenary session, and, workshops in EEG, EMG and transcranial magnetic stimulation. Again, we have important guests who have accepted our invitation for this event.

So we are expecting two days of intense scientific activity, in a beautiful environment, and maybe will take a few minutes to enjoy the beautiful beach and the sea, to chat, to make new friends.

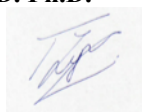
Welcome to the 7<sup>th</sup> Edition of the Summer School in Clinical Neurophysiology !

Sincerely,

**Tudor Lupescu M.D. Ph.D.**

*ASNER President*

*contact@asner.org*



<http://www.asner.org>

<https://www.facebook.com/asner.org/>

**Ioana Mindruta, M.D. Ph.D.**

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**Mihai Moldovan, MD, PhD**

*ASNER Scientific director*

Copenhagen University, Denmark and "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

*moldovan@sund.ku.dk*

### **Friday July 8th**

12.00 - 13.00 Welcome cocktail

13.00 - 13.15 - Opening remarks

#### **13.15 - 15.15 EEG workshop (Chair Ioana Mindruta)**

Activation procedures in EEG recordings and maturation of EEG rhythms - Dana Craiu, Bucharest, Romania

Vegetative seizures - need for additional electrodes in the EEG protocols - Oana Tarta, Bucharest, Romania

Source localisation method - Mihai Malaia, Bucharest, Romania

EEG recordings

*15.15 - 15.45 Coffee Break*

#### **15.45 - 18.30 EMG workshop (Chair Ana-Maria Cobzaru)**

Miller Fisher Variant of Guillain-Barre Syndrome: A Case Report – Ionela Codita

Subacute tetraparesis with axonal polyneuropathy - a tricky differential diagnosis -Anca Adriana Arbune. Ana-Maria Cobzaru, Cristina Tiu

Asymmetrical amyotrophy of the small muscles of the hand A historical retrospective of diagnosis and therapy as homage to our professors – Mircea Moldovan

EMG recordings

**Free time**

### **Saturday, July 9th**

#### **Plenary Session 1 (Chair Tudor Lupescu)**

9.00 - 9.45 Vagus Nerve Stimulation - Criteria of patient selection - Nicola Specchio, Roma, Italy

9.45 - 10.15 SEEG guided RFTC for drug resistant epilepsy - Ioana Mindruta, Mihai Malaia, Irina Popa, Cristian Donos, Jean Ciurea, Alin Rasina, Andrei Barborica.

*10.15 - 10.30 Coffee break*

#### **Plenary Session 2 (Chair Mihai Moldovan)**

10.30 - 11.15 Restless legs syndrome - Mauro Manconi, Lugano, Switzerland

11.15 - 12.00 Transcranial Direct Electrical Stimulation - Basics - Andrea Antal, Gottingen, Germany

12.00 - 12.30 TMS in neurological disorders - Tudor Lupescu, Bucharest, Romania

12.30 - 13.00 'Safety factor for conduction' of peripheral axons - Mihai Moldovan, Copenhagen, Denmark

*13.00-14.00 - Lunch*

14.00 - 14.30 Sympozion Genzyme

14.30 - 15.00 Sympozion Merck

15.00 - 15.15 Coffee break

15.15 - 16.15 Sleep lab: case presentations and discussions

Sleep-related movement disorders (Mauro Manconi)

Motor behaviors during sleep (Floriana Boghez)

16.15- 18.30 EMG workshop

TDCS (Andrea Antal)

Ultrasound (Pavel Bogdan)

19.00 Get together dinner

### **Sunday, July 10th**

#### **9.00-12.00 cases/presentations from the audience (Chair Ionela Codita)**

Optic nerve assessment identify biomarkers of axonal pathology in multiple sclerosis – Simona Petrescu

Visual evoked potentials – the influence of technical recording factors – Mircea Moldovan

Hypometabolism on PET imaging of epileptic patients – SOZ or hubs of the epileptogenic network? - Anca Adriana Arbune

**TRANSCRANIAL MAGNETIC STIMULATION**  
**- principles, technique, applications**

Tudor Lupescu,

*Agrippa Ionescu Hospital, Bucharest*

*RoNeuro Institute for Neurological Research and Diagnosis*

The presentation consists of some interesting electroneuromyographic results and their correlation with the clinical examination, in order to provide examples of good clinical reasoning that leads to a correct evaluation and diagnosis. All the examples originate from the author's own clinical experience.

**Tudor Dimitrie Lupescu**  
**MD, Ph.D.**

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Tudor Lupescu obtained his medical degree from “Carol Davila” University of Medicine in Bucharest, in 1989. After 3 years of training at Colentina Clinical Hospital he became Specialist in Neurology in 1994. Since 2006 he is running the Neurology Department at Agrippa Ionescu Hospital in Bucharest. 1998, he qualified as Consultant Neurologist. Since his early years of training in Neurology, Tudor Lupescu has shown a special interest in Clinical Neurophysiology. In 2000 he earned a Competence in Clinical Neurophysiology (EEG, EMG, and Evoked Potentials). 1997 he was the first to use Transcranial Magnetic Stimulation in Romania. This was also the subject of his PhD thesis presented in 2005. Since 2008, Tudor Lupescu is President of ASNER – Romanian Society of Electrodiagnostic Neurophysiology. He is also founding member and vicepresident of the the Romanian Society of Diabetic Neuropathy.

Dr Tudor Lupescu is associate member of the American Academy of Neurology, and associate member of the American Association of Neuromuscular and Electrodiagnostic Medicine. Between 2008 and 2014 he was also member of the Neurophysiology Subcommittee of ENS, and since 2015, he is member of the Neurophysiology Subcommittee of the European Academy of Neurology.



## Restless legs syndrome

Mauro Manconi,

*Neurocenter of the Southern Switzerland of Lugano,  
Civic Hospital (Lugano, Switzerland)*

**Mauro Manconi MD, Ph.D.**

**Assoc. Prof.**

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Restless legs syndrome (RLS) is a common sensorimotor disorder characterized by an unpleasant sensation in the limbs that appears or worsens during rest and night-time and disappears or improves by movement. Other frequently associated features are insomnia, positive family history, periodic leg movements during sleep (PLMS) and response to dopamine-agonist treatment. Preferential D3 selective dopamine-agonists are considered the first line treatment in RLS, they improve the sensory symptoms and suppress PLMS even at very low doses and since the first night of administration.

PLMS are repetitive leg jerks characterized by a flexion movement at ankle, knee and hip, which arise from sleep and are recorded by placing two surface electrodes on each tibialis anterior muscle in a polysomnographic (PSG) context. Contractions lasting from 0.5 to 10 seconds, separated by an inter-movement interval ranging between 5 and 90 seconds, and occurring at least four in a row, belong to the PLMS category. Approximately 90% of RLS patients present PLMS; however, PLMS can also be observed in other neurological or sleep disorders and in healthy adult/elderly subjects. Only PLMS with intermovement interval around 10-40 s respond dramatically to dopamine-agonists; on the contrary, other leg movements during sleep separated by intervals approximately <5 s or >50 s and isolated leg movements are not modified, probably because they are not under dopaminergic control.

PLMS are associated with cortical (electroencephalography, EEG) arousals and autonomic sympathetic (heart rate variability, HRV; arterial blood pressure) activations. Insomnia, on one side, and the increased cardiovascular risk recently observed in RLS patients on the other, are suspected to be the direct clinical consequence of these cortical and autonomic activations that can occur chronically for years. PLMS can be associated with insomnia at night or daytime hypersomnia even in the absence of RLS symptoms, in the context of the so-called periodic limb movement disorder. Moreover, the cardiovascular risk, especially hypertension, seems to be correlated more with PLMS than with RLS.

**Associate Professor in Neurology.** National Concourse, from the Italian Ministry of University.

**Head of the Service** at the Neurocenter of the Southern Switzerland of Lugano, Civic Hospital (Lugano, Switzerland). He is the responsible of the Sleep and Epilepsy Center, coordinating a clinical team (5 MDs, 8 Technicians), a clinical research team (2 PostHoc), and a basic research team (2 Post Hoc)

Principal Investigator: “**Swiss National Foundation**”, competitive National Grant. Perinatal depression: chronobiology, sleep related risk factor and light therapy. Identification Number: 320030\_160250 / 1 (525.000 CHF).

Co-Investigator: “**Swiss National Foundation**”, competitive National Grant. Infra-slow oscillations during sleep, after acute sleep deprivation, and in patients with restless legs syndrome/periodic leg movements during sleep (RLS/PLMS).

Head of the Service at the Sleep Center of the Neurocenter of Lugano, Civic Hospital, Switzerland.

The main field of my research regards sleep disorders, particularly sleep related movement disorders, such as restless legs syndrome (RLS) and periodic limb movements (PLM).

Despite these considerations, the pathological meaning of PLMS is still controversial. Are PLMS the cause of cortical and autonomic oscillations? Are PLMS the consequence of one or both of the other two phenomena? Are all of these phenomena simply synchronized but not directly related? The availability of powerful pharmacological suppressors of PLMS – dopamine agonists – makes it crucial to clarify if there is a causal relationship or a sort of hierarchic organization of these three categories of events (cortical, autonomic, and motor) and, possibly, to characterize its direction.

## Vagal nerve stimulation: indications and outcome.

Nicola Specchio

Nicola Specchio

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*Bambino Gesù Children's Hospital, IRCCS, Rome, Italy*

Vagus nerve stimulation (VNS) is a worldwide applied technique for the treatment of intractable epilepsy that cannot benefit from resective surgery. Recent clinically-controlled trials have reported a 50% seizure control rate in about 30% of patients'. However, its efficacy seems to vary among teams and the type of patients who can benefit from this technique is so far unknown

This safe, simple, and adjustable technique reduces the number of seizures and multiple publications support its increasing efficacy and effectiveness, with few adverse effects. The goal of the use of VNS would significantly increase whether the efficacy of this procedure and the factors predicting a response, would be known in details. Particularly the question is who are the best candidates for VNS implantation.

VNS is not a cure, and the total elimination of seizures is rare. However, many people who undergo VNS experience a significant (more than 50%) reduction in the frequency of seizures, as well as a decrease in seizure severity. This can greatly improve the quality of life for people with epilepsy.

Cleveland clinic group performed an experimental trial in the kainic acid limbic model of epilepsy in rats treated by VNS stimulation using the same parameters usually used in humans.

The group from Ghent in Belgium have very recently reported the effect of VNS in amygdala-kindled seizures in rats. When left VNS was applied 2s after induction of the kindling stimulus the mean after discharge duration was significantly reduced after a 60 s VNS train compared to the control situation (50% reduction approximately).

Patients with epilepsy uncontrolled by anticonvulsant medications may be candidates for VNS. The definition of medically intractable generally includes a description of an adequate drug trial without unacceptable side effects. Moreover it should be stated that candidates to VNS should have been carefully evaluated and excluded from respective epilepsy surgery.

In 1999 I graduated in Medicine at the University of Bari, Bari, Italy. Research collaboration started in 1994. Between 1999 and 2004 I trained as a Neurologist at the Neurological Institute of the University of Bari, attending the general neurological ward, the Centre for the Study and Treatment of Epilepsy and the laboratory of neurophysiology. In 2004 I enrolled for a PhD course in Neuroscience at the "Department of Neurological and Psychiatric Science, University of Bari, Italy. From 2008 to 2013 I had a Full position as a Consultant at Division of Neurology, Bambino Gesù Children Hospital, Roma.

From the 2011 I am tutor for the Virtual Epilepsy Academy (VIREPA) of the International League Against Epilepsy leading the course on non-epileptic paroxysmal disorders.

From 2014 I am Head of Epilepsy Surgery Unit at Department of Neuroscience, Bambino Gesù Children's Hospital.

I participated as invited speaker to several national and international congresses and workshops, and more recently to the 10<sup>th</sup> and 11<sup>th</sup> European Congress of Epilepsy (ECE) and to the 31<sup>st</sup> International Epilepsy Congress (IEC)

For the period 2011-2014 and 2014-2017 I was elected to the Board of Directors of the Italian League Against Epilepsy.

The patient and family should be educated about the nature of the device being implanted. This includes a discussion of the expectations of the patient and the reality that they will likely not be seizure free.

VNS has been investigated in pediatric patients with epileptic encephalopathies, Lennox-Gastaut syndrome, tuberous sclerosis, hypothalamic hamartomas and Landau-Kleffner syndrome.

More recently has been approved and commercialized a closed loop system of VNS (Aspire®) that automatically deliver an extra stimulation as far as it reveal an ictal tachycardia. This method might increase the chance of interrupting seizures and the overall outcome of implanted patient.

**Transcranial direct current stimulation (tDCS): possibilities, clinical applications and common pitfalls**

Andrea Antal

*Department of Clinical Neurophysiology  
University Medical Center, Göttingen, Germany*

Neuroplasticity became one central topic of neuroscience research in the last decades. Dynamic modifications of neuronal networks are an important substrate for learning and memory formation. Pathological neuroplasticity might be one foundation of numerous central nervous system diseases. Transcranial direct current stimulation (tDCS) was developed by our group as a non-invasive tool to induce neuroplasticity in the human cerebral cortex. tDCS as a tool aims to induce prolonged neuronal excitability and activity alterations in the human brain via alterations of the neuronal membrane potential. Accordingly, tDCS in the human is a promising tool in the treatment of diseases that are accompanied by changes of cortical excitability. tDCS seems also to be an efficient tool to alter learning and cognitive performance in healthy humans. The effects have been most extensively tested for the motor cortex stimulation. Unfortunately the results of the different studies are not always consistent. It was frequently observed that the efficacy and direction of the effects depends on the timing of stimulation, electrode arrangement, and task characteristics, besides anatomical and physiological factors. Future studies systematically probing the stimulation parameters and developing new protocols are needed to explore the reasons for the inconsistencies.

**Prof. Dr. Antal, Andrea**

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Extraordinary Professor, Dept. of Clinical Neurophysiology, University Medical Center, Göttingen

2005 Habilitation, Cognitive Neuroscience, Georg August University Göttingen

1998 PhD, Biological Sciences, Albert Szent-Györgyi University (Hungary)

1993 Dr. univ., Comparative Physiology, József Attila University of Szeged, (Hungary)

1990 Graduation in Molecular Biology and Biotechnology, József Attila University of Szeged (Hungary)

Research areas (present and past):

Transcranial stimulation, Neuroplasticity, Neurodegenerative disorders, Parkinson's disease, chronic pain, Migraine



## Intermittent light stimulation method (ILS)

Dana Craiu

Prof. Dana Craiu. MD

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*Carol Davila" University of Medicine, Pediatric Neurology Clinic, Al Obregia Hospital, Bucharest, Romania*

ILS is a stimulation method that is obligatory to be performed, along to hyperventilation during standard EEG (electroencephalogram) recording. It can be performed using a stroboscope with variable frequencies, between 1 and, ideal, 60 Hz in three different situations: at eyes closure, with eyes closed and with eyes open for each frequency. Another method may be the use of disks with stripes having different diameters. clinical examples are presented and interactively discussed aiming to underline tips and tricks of performing and interpreting ILS.

## Maturation of EEG rhythms

EEG interpretation may be very difficult in children if the age of the patient is not specified. If the reader knows the milestones of EEG maturation, may even appreciate the age of the subject. We present the EEG changes induced by brain maturation and EEG variability in different subjects at the same age. The presentation will bring data from the statistical studies offering the normal limits of the frequencies in different ages. Interactive discussions with participants aiming identification of maturational aspects of the EEG at different ages are intended.

Dana Craiu is Professor of Pediatric Neurology at "Carol Davila" University of Medicine Bucharest. She is a member of the EPNS Board (European Pediatric Neurology Society) since 13 years ago and Chair of TAB (European Training Advisory Board for Pediatric Neurology) si al CNA (European Commission of National Advisors for Pediatric Neurology). Since 2010 she is Chairing the Education Commission of SRNP (Romanian Society of Pediatric Neurology), and since 2015 is President of SRIE (Romanian Society Against Epilepsy).

She is specialized in EEG, Epileptology, video-EEG and presurgical investigation for epilepsy surgery after numerous courses offered by ILAE (Basic EEG, Pediatric EEG, Epilepsy treatment), San Servolo epileptology courses (2006 Epilepsy surgery, 2007 Epileptology in children, 2012 Epileptology in children - trainer), Postdoctoral Fellowship in Heemstede, The Netherlands, for EEG, video-EEG, presurgical evaluation for epilepsy surgery.

In present she is trainer VIREPA in Basic EEG ILAE course.

## Vegetative signs in epileptic seizures

Oana Tarta Arsene, MD



Oana Tarta-Arsene, Cristina Pomeran, Cristina Motoescu, Dana Craiu

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*Departamentul de Neurologie Pediatrica, Spitalul Clinic de Psihiatrie 'Al Obregia', Bucuresti, Romania*

MD PhD, Pediatric Neurologist, Senior Doctor, Junior Lecturer, Secretary of the Romanian Chapter – International League Against Epilepsy, Bucharest, Romania

Vegetative signs in epilepsy are an important tool for understanding semiology and life-threatening complications of the seizures and also for positive and differential diagnosis with other paroxysmal non-epileptic events.

Depending on localization and lateralization of the epileptic focus, these could be cardiac, respiratory, pupillary, gastro-intestinal or many others.

This presentation will present a short review of different clinical signs of seizures with video-EEG recordings and it will outline the importance of using poly-graphic recordings for positive diagnosis.

Dr Oana Tarta-Arsene received his Medical Degree from the 'Carol Davila' University of Medicine and Pharmacy University, Bucharest, Romania. She had her resident ship in Pediatric Neurology (2000-2005) under the supervision of Professor of Pediatric Neurology S. Magureanu, awarded as Honorary Member of European Pediatric Neurology Society. During this period she was also teaching assistant in the Department of Pediatric Neurology, 'Carol Davila' University of Medicine and Pharmacy, and then junior lecturer from 2005.

She is certified as pediatric neurologist from 2005, and from then she is working in a Romanian Referral Center for Pediatric Neurology, her specialization being focused to epilepsy and from almost 10 years in epilepsy surgery. She is well-trained in epilepsy, having completed a lot of national and international courses in this field, especially in EEG. Her knowledge is covered by a lot of practical work, because she is reading long term monitoring video-EEGs which are made in her department, from almost 10 years.

Her Phd Thesis was also focused on epilepsy, having as title "The contribution of Functional magnetic resonance imagery in assesment of language area of children with non-lesional focal epilepsy" and being finished in 2012.

## SEEG guided radiofrequency-thermocoagulation: a potential standard method for pre-resection evaluation

Ioana Mindruta, Mihai Malaia, Irina Popa, Cristian Donos, Jean Ciurea, Alin Rasina, Andrei Barborica.

*Neurology Department, “Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania*

*University of Physics, Bucharest Romania*

*Bagdasar Arseni Hospital, Functional Neurosurgery Department, Bucharest Romania*

**Introduction:** Minimally invasive techniques in epilepsy surgery offer many advantages to conventional surgery including addressability, cost reductions and a decrease in primary and secondary morbidity. (Quigg and Hardy, 2014) Radiofrequency thermocoagulation (RFTC) on the same depth electrodes used for diagnosis has been demonstrated to be safe and moderately effective (Guenot 2004, 2008, 2011; Catenoix 2008, 2015) although a limited number of centers have reported their series. We address this by presenting the initial results obtained in our center.

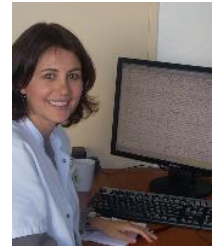
**Methods:** 8 patients received RFTC treatment at the end of their SEEG procedure from Jan. 2015 to April 2016. Lesions were produced between 2 contiguous contacts on depth electrodes (Dixi, Besancon, FR) implanted with custom (FHC Inc, Maine, USA) and standard (Leksell, Elekta, Stockholm, SW) stereotactic frames allowing reaching most difficult targets. A 50-V, 120-mA current was applied for 10 to 40 seconds to reach an estimated temperature of 78-82 C. Tissue impedance was monitored throughout the procedure. Contacts in the cortex showing low voltage fast activity or spike and wave activity at seizure onset were targeted. Prior physiologic responses obtained at direct electrical stimulation (DES) were an exclusion criteria. Lesions' morphology was estimated at 3 months with post-procedure MRI.

**Results:** 2 to 10 contact pairs were coagulated per procedure (6 patients had frontal epilepsy, 1 occipital and 1 opercular). 6 were MRI negative cases – classically not viewed as candidates for RFCT, while 2 showed a malformation of cortical development aspect. Median follow-up was 6 months (range 1-15). 3 (37%) are seizure free (Engel I A), 4 (50%) experienced a significant improvement in either seizure frequency or seizure duration (Engel III) 2 of which after an initial seizure free period, while 1 (13%) obtained no benefit. No acute or long-term complications were registered.

**Ioana Mindruta**

**Lecturer, MD, PhD**

ioanamindruta@me.com



47-year old, neurologist, with competence in electrophysiology and special interest in epileptology, mainly presurgical exploration for epilepsy surgery. PhD thesis on “Sleep studies in epileptic syndromes” in 2006.

Current position at the University Emergency Hospital in Bucharest in the Epilepsy and Sleep Monitoring Unit and also hospital coordinator of the National Programs for Pharmacoresistant Epilepsy and Rare Disorders.

Academic affiliation - lecturer in neurology at the University of Medicine and Pharmacy “Carol Davila” of Bucharest.

Vicepresident of Romanian Association for Clinical Electrodiagnosis (ASNER) since 2009 and member in the board of Romanian Society of Neurology since 2013.

**Conclusions:** Our early experience, confirms the technique's safety profile and efficiency, even in a difficult non-lesional population. A significant impact on the seizure frequency after RFCT could have a prognostic value on the chances for open surgery to successfully interfere with the alleged epileptogenic network or even avoid one.

## **Miller Fisher Variant of Guillain-Barre Syndrome: A Case Report**

Ionela Codita

*Neurology Department of Elias University Emergency Hospital, Bucharest*

*Ionela Codita*

*MD, PhD*

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**Background:** Miller Fisher Syndrome is an immune mediated neuropathy characterized by ataxia, areflexia and ophthalmoplegia, with a monophasic , self-limited course and spontaneous improvement.

**Case report:** The authors present a 48-year-old female with limb ataxia ( > left) , gaze palsy , unilateral weakness and areflexia. The symptoms developed within 7 days. The brain MRI was normal. Nerve conduction studies revealed reduced amplitude of SNAPs and abnormalities in the patient's blink response. A high titer of antiGQ1b was detected . An intravenous immunoglobulin was given and the patient gradually improved.

**Conclusion:** The presented case was atypical in its clinical course and treatment. It could support a theory of the continuity between Miller Fisher Syndrome and Guillain-Barre Syndrome. Early correct diagnosis is important and avoids unnecessary investigations and guides appropriate use of immunotherapy.

Ionela Codita is currently working as a Senior Neurologist in the Neurology Department of Elias University Emergency Hospital in Bucharest. She has graduated “Carol Davila” University of Medicine and Pharmacy in 1995 and became a specialist in Neurology in 2000.

She earned a Competence in Clinical Neurophysiology in 2005. During her practice, dr. Codita attended many courses and teaching programs in the field of Clinical Neurophysiology such as: scholarship in Neurophysiopathology field at Policlinical Institute of San Donato Milanese, Italy (2002-2004), training Course in EMG and Neurography Uppsala , Sweden (2009), International SFEMG and QEMG Course –Kobe, Japan (2010), VIREPA distance learning courses on “EEG in the diagnosis and management of epilepsy – Basic Course 6th edition” (September 2011- March 2012) and “EEG SCORE course-1st edition”( November 2012-March 2013), the international educational course “Dianalund Summer School on EEG and Epilepsy” (July 2012).

She also manifests interest in Epilepsy, Motor Neuron Diseases and Movement Disorders. Dr. Ionela Codita is a member of the Romanian Society of Neurology, affiliated to the ENFS (European Federation of Neurological Societies) and to the WFN (World Federation of Neurology) and since May 2013 she is the secretary of ASNER-The Romanian Society of Electrodiagnostic Neurophysiology.

## **‘Safety factor for conduction’ of peripheral axons**

Mihai Moldovan (1,2)

1) *Copenhagen University DK*; 2) *Carol Davila University, Bucharest, RO*

Myelinated peripheral axons are biological structures specialized in energy-efficient conduction of action potentials. Axonal conduction involves a complicated voltage-gated ion channel machinery comprised of several types of Na<sup>+</sup> channels (mediating the inward depolarizing currents), K<sup>+</sup> channels (mediating the outward rectifying currents) and hyperpolarization-activated cyclic nucleotide-gated channels (mediating the inward rectifying currents), as well as energy-dependent pumping mechanisms required to maintain the ionic concentration gradients across the membranes. Additionally, the spatial distribution of these channels is tightly controlled by axon-Schwann cell interactions.

The complicated axonal machinery ensures that conduction can occur in conditions of alterations in near nerve environment such as variations in ion channel concentrations or temperature. The ‘safety factor for conduction’ was introduced as a concept to explain the 5 x larger voltage-gated Na channel density than required for ‘saltatory conduction’ which e.g. can explain maintenance of peripheral conduction during antiepileptic Na<sup>+</sup> channel blocker treatment, or preservation of conduction in partial demyelination. Nevertheless recent developments indicate that the safety factor for conduction is also capable of a tremendous plasticity according to nerve activity levels. Different nerves can have different safety factors and along the same nerve the safety factor can differ.

This presentation reviews recent work in my lab on safety factor plasticity in normal and demyelinated nerves and their implications for electrodiagnosis of conduction failure. Furthermore, this work raises hope for developing new therapeutic strategies for improvement of axonal conduction, with implications for both peripheral and central axons.

**Mihai Moldovan**

**Assoc. Prof., MD, Ph.D.**

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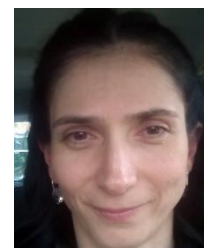


Mihai Moldovan obtained his medical degree from “Carol Davila” University Bucharest in 1999. Based on his research interests as a student, after graduation he was selected to work in the group of prof. Christian Krarup that continues the Copenhagen neurophysiology school founded by prof. Fritz Buchthal in the 60’ with the aim of translating experimental neurophysiology into clinical electrodiagnostic procedures for patients with nerve and muscle disease. Mihai Moldovan obtained his PhD degree in neurophysiology from Copenhagen University in 2004 where he continues his scientific career as associate professor. His research is focused on distinguishing the contribution of voltage-gated ion channel dysfunction to pathophysiology of neurodegenerative disorders, with particular emphasis on peripheral nerve excitability testing. While based in Copenhagen, Mihai Moldovan continued to collaborate with prof. Leon Zagrean at “Carol Davila” University, Department of Physiology and Neuroscience. In 2011, he founded the COMAEEG.RO international network, bringing together Romanian neuroscientists, clinicians and engineers dedicated to improving the monitoring of the comatose brain excitability. Emerging from these wide research interests are not only original publications and review articles in international journals but also educational chapters in neuroscience and neurophysiology textbooks in Romanian language. Mihai Moldovan is a member of the editorial board member for Clinical Neurophysiology, the official scientific journal of the International Federation of Clinical Neurophysiology (IFCN) and has scientific duties in several international organizations including International Brain Research Organization (IBRO) and the European Federation of Neuroscience Societies (FENS). He is also founder and acting president of the National Neuroscience Society of Romania (SNN) and founder of the Romanian Society of Electrodiagnostic Neurophysiology (ASNER) for which he now serves as scientific director. For his activity he received several international and national prizes, most recently the 2016 ‘P.K.Thomas’ prize of the European Academy of Neurology.



## Optic nerve assessment identify biomarkers of axonal pathology in multiple sclerosis

Simona Petrescu



Simona Petrescu

*Neurology Department of Elias University Emergency Hospital, Bucharest*

senior neurologist

The Emergency University Elias Hospital

### Purpose of the study:

Our aim was to identify possible correlations between physical disabilities assessed by expanded disability status score (EDSS) and neurodegenerative process measured by retinal nerve fibers thickness, and also with demyelization process measured by visual evoked potential with P100 wave latency at optic nerve level on patients diagnosed with multiple sclerosis (MS).

This study wants to find a structural biomarker at central nerve system (CNS) level which could correlate with clinical disability. The optic nerve is an accessible structure of CNS easy to investigate. It can offer this answer.

### Methods:

We analyzed a population of 111 patients diagnosed with different clinical forms of multiple sclerosis based on 2005 revised Mc Donald criteria, for whom we assessed clinical disability by EDSS, and by different subscales of multiple sclerosis composite (MSFC) as timed to walk 25 foot (TW25F) and nine hole peg test (9HPT).

Optic nerve involvement was assessed for each eye measuring visual acuity (VA) (Snellen chart), P100 wave latency by visual evoked potential (VEP) and retinal nerve fiber layer thickness (RNFL) by optical coherence tomography (OCT).

### Results:

The medium age of our population was 38.09 and the medium EDSS was 3.3. 76 out of 111 were women.

79 patients were diagnosed with relapsing remitting (RR) MS, 7 with clinically isolated syndrome (CIS), the other were diagnosed with progressive form of MS: 7 with primary progressive MS and one with primary progressive with relapse MS.

We obtained positive correlations, and statistically significant between EDSS and 9HPT for dominant hand ( $r=0.58$ ,  $p=0.0001$ ) and also for non dominant hand ( $r=0.66$ ,  $p=0.0001$ ) using Pearson correlation.

EDSS score correlates statistically significant with P100 wave latency and visual acuity for both eyes using Pearson correlation, so we obtained negative correlation between EDSS and VA for right eye ( $r=-0.45$ ,  $p=0.0001$ ), and for left eye ( $r=-0.49$ ,  $p=0.0001$ ).

We also observed statistically significant positive correlation between EDSS and P100 wave latency for right eye ( $r=0.405$ ,  $p=0.0001$ ), and left eye ( $r=0.400$ ,  $p=0.0001$ ).

RNFL doesn't correlate with EDSS, VA or P100 wave latency. Using chi square correlation between EDSS score (we choose a cut of value of 3) and pathological value of RNFL by OCT we didn't obtain a statistical significant result. The results were: for right eye  $\phi=0.01$ ,  $p=0.9$ , and for left eye ( $\phi=-0.1$ ,  $p=0.3$ ). Similar results were obtained for EDSS of 4.0. The results were: for right eye ( $\phi=-0.009$ ,  $p=0.9$ ), and for left eye ( $\phi=0.017$ ,  $p=0.8$ ).

### Discussion:

In order to understand the pathology of multiple sclerosis the anterior optic nerve pathway offers an attractive model.

Optic nerve assessment can be realized through non invasive complementary methods. Functional and structural data of optic nerve can be obtained by VA measurement, VEP and OCT assessments.

Our study shows that axonal pathology of the optic nerve (part of CNS exclusively composed by white matter) correlates with clinical disability measured by EDSS, suggesting that P100 latency is a functional biomarker of the disease.

It is needed a prospective study to validate such a marker of the progression of the disease.

## Peripheral nerve ultrasound workshop

Pavel Bogdan, MD, PhD



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Assistant professor, Physiology and Neurosciences  
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The 1-hour workshop will consist of

A brief theoretical introduction in ultrasound and  
ultrasound anatomy for peripheral nerve and nervous  
plexus (20 min)

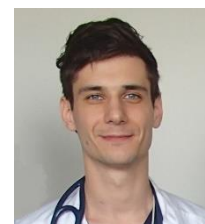
Practical demonstrations (40 min).

2014 PhD at UMF “Carol Davila” , Bucharest,  
Romania

2013 DESA – Diplomate of the European Society of  
Anesthesiology - Viena, septembrie 2013

Young Teachers’s Grant (Societatea Europeana de  
Anestezie) – Milano, Congresul Euroanesthesia 2009

2006 MD at “Ovidius” University Constanta,  
Romania

**Interictal and ictal electrical source imaging: principles and practical demonstration****Malaia Dragos-Mihai, MD**Mihai Dragos Maliia<sup>2</sup>,

mihaidragosh@yahoo.com

Cristian Donos<sup>1</sup>, Ioana Mindruta<sup>2,3</sup>, Andrei Barborica<sup>1</sup>

<sup>1</sup>Physics Department, University of Bucharest, Bucharest, Romania <sup>2</sup>Neurology Department, University Emergency Hospital, Bucharest, Romania <sup>3</sup>Neurology Department, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania <sup>4</sup>FHC Inc, Bowdoin ME, USA

Correctly solving the inverse problem in EEG is probably the most useful electrophysiological skill in epileptology. That is why electrical source imaging has emerged as a leading post-processing procedure, being routinely employed in more than half of the European tertiary centers for epilepsy. A wide range of software each implementing a multitude of algorithms are available on the market, many being open-access, however the scarcity of well-designed studies in the field makes an informed choice between them problematic. My part of the EEG-workshop will try to offer a brief introduction into the electrophysiological principles and the correct implementation of these techniques followed by a practical demonstration session. A series of interictal spikes as well as the rhythmic epileptiform discharges at the ictal debut belonging to a candidate for epilepsy surgery will be uploaded and analyzed live with Brainstorm, an open access platform with a powerful tutorial library and online community. The results will be compared with the intracranial solutions as obtained by the depth electrodes implantation (stereoelectroencephalography) in the SUUB laboratory. The participants are invited to take part in the demonstration and to later try these analyses and discuss the solutions obtained on their own cases.

28 year old, 3rd year neurology intern at the University Emergency Hospital Bucharest with a special interest in epileptology. Graduated UMF "Carol Davila" Bucharest with honors (3rd of my promotion). Involved in the Romanian Epilepsy Surgery Program with work and experience focused upon presurgical evaluation, implantation design via the SEEG technique, invasive monitoring and direct electrical stimulation, resection proposal, intraoperative functional mapping and postoperative follow up. Completed 2 grants: 3 months EAN Department to Department Co-operation in Freiburg Epilepsiezentrum, Germany and 6 months IFCN Research Award in Danish Epilepsy Center, Dianalund, Denmark. Member of International League against Epilepsy, International Federation of Clinical Neurophysiology and Epilepsy Consortium. Research interest in electrophysiology, in particular connectomics, brain mapping, biomarkers of the epileptogenic zone and electrical source imaging. Published original research abstracts and articles, one book chapter and held awarded speeches at European events in the field. As non-medical interests I am passionate about all fields of cognitive sciences but especially keen on the study of consciousness and the philosophical literature derived from it.

### **Subacute tetraparesis with axonal polyneuropathy - a tricky differential diagnosis**

Anca Adriana Arbune, Ana-Maria Cobzaru, Cristina Tiu

*Neurology Department, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania*

Tetraplegia with progressive onset in young patients gives rise to multiple differential diagnoses, varying from Guillan Barre syndrome to hypoglycemia, requiring a detailed clinical examination, extensive workup and careful anamnesis. We present the cases of two young males (31 and 37 years old) with tetraparesis with progressive onset, admitted and treated in the Neurology Clinic of, the University Emergency Hospital, Bucharest in 2015. The patients developed tetraparesis progressively over 4 weeks. Accompanying symptoms were hypochoemic microcytic anemia, increased bilirubin levels, mild inflammatory syndrome, in the absence of fever. Both patients reported weight loss and abdominal pain prior to hospitalization. which was misinterpreted as a renal colic in one case and as enterocolitis in the other. The clinical examination revealed loss of reflexes, tetraparesis with predominant involvement of proximal muscles with the sparing of sensitivity, and in one case, extensive amiotrophy . The electrophysiological examination confirmed motor axonal polyneuropathy.

### **Motor behaviors during sleep**

Floriana Boghez\*, Ioana Mindruta

*\*Clinica Academica, Bucharest, Romania*

Sleep represents one third of our 24-hour cycle and almost any sleep disorder affects quality of life. There has been described almost 100 sleep diseases and many of these sleep disturbances involve a motor component: from periodic limb movements to nocturnal seizure and parasomnia behaviors. Sleep-related movement disorders are relatively simple and stereotyped movements that occur during sleep or at its onset. Restless leg syndrome (RLS) and periodic limb movement (PLM) disorder are the most frequent among them and sleep complaints and/or daytime somnolence are the consequences of these disturbances. Neurophysiology can be very helpful with the diagnosis because polysomnography (PSG) is the gold standard for the PLM syndrome diagnosis and its severity.

Ana-Maria Cobzaru

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Neurologist with competence in electrophysiology and special interest in clinical neurophysiology working in the University Emergency Hospital in Bucharest as general neurologist and in private sector as neurophysiologist.

The patients were referred to our hospital as possible subacute polyradiculoneuritis for treatment with ivIG, but more thorough investigations revealed acute intermittent porphyria and lead intoxication. The particularity of the cases is the presentation of tetraparesis as main manifestation in acute intermittent porphyria, in one case induced by lead intoxication, and in the other, the late onset of the first attack determined by lead exposure. The differentiation between demyelating and axonal polyneuropathies can only be done through electrophysiological examination. Acute intermittent porphyria must always be taken into consideration as differential diagnosis of subacute tetraparesis and detailed anamnesis can bring out the precipitating factors.

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Neurologist with competence in electrophysiology and special interest in clinical neurophysiology working in the Clinica Academica.

During sleep, more complex motor phenomena can occur and in neurology practice we often find out about nocturnal seizures in our patients. When their clinical aspect is not tonico-clonic but more bizarre, we might also think at parasomnias, which are disorders characterized by the occurrence of complex motor behavioral events or experiences at sleep onset, within sleep or during arousal from sleep. It happens frequently to resemble nocturnal seizures and sometimes the differential diagnosis can be hard. Night video-EEG and PSG should be reserved for the cases in which the diagnosis is still unclear after a careful history and physical examination.

**Asymmetrical amyotrophy of the small muscles of the hand A historical retrospective of diagnosis and therapy as homage to our professors**

Mircea Moldovan, Ionela Codita, E Georgescu

*Neurology Department of Elias University Emergency Hospital, Bucharest*

The 74 yrs old patient was first examined by a neurologist in 1960, for loss of strength in the left hand, accompanied by amyotrophies of the small muscles.

Diagnosed with cervical rib syndrome, she underwent bilateral cervical surgery in 1960 and 1961.

In 1976, the persistence of the symptoms at the left hand, together with the onset of a discrete amiotrophy of the right hand, warranted a new set of investigations, comprising a rachidian aerography and a myelography with lipiodol, which were normal.

Reconsidering the symptomatology, the patient was operated for a right side scalen syndrome.

Repeated neurographic and EMG examinations in 1976, 1978, 1983 and 1984 have evidenced – with small variations – an aspect of denervation in the small muscles of the left hand, and a discrete denervation in the right hand, with a prolonged distal latency of the right median nerve.

The differential envisaged syndromes of compression of the brachial plexus, siringomyelia, CMT disease, motor neuron disease, monomyelinic amyotrophy, which were discarded.

About 20 years after debut, in 1983, with a stationary neurological symptomatology, the hypothesis of a monomyelinic atrophy type O'Sullivan was formulated.

Prof Dr V Voiculescu appreciated the association of the sensitivity disorders of the left forearm with the amiotrophy as being determined by a partial lesion of the left brachial plexus, secondary to a calcificated fibrosis of the left lung apex after a therapeutic pneumothorax at 9 year of age.

Stabilized for 40 years, the patient returned to be consulted subsequent to the onset of pain and paresthesia in the fingers of the right hand, as well as MRI evidenced degenerative alterations of the cervical spine.

**Mircea Moldovan**

**MD, PhD**

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Dr. Mircea Moldovan, graduate of the “Carol Davila” University Bucharest, Doctor of Medical Sciences, MD is a neurologist at the Hospital “Elias” Bucharest since 1968. Throughout his career, he had a continuous interest for clinical neurophysiology. In the 80s, his main interest was the EEG and evoked potentials under the guidance of Prof Dr V Voiculescu. In the 90s, his interest expanded to the peripheral conduction studies and EMG. During his pioneering work in Romanian clinical neurophysiology, Mircea Moldovan advocated the diagnostic importance of clinical neurophysiology for neurological practice through talks at national scientific meetings and scientific publications. Most importantly, however, through his wealth of practical experience and didactic spirit, he helped initiate in clinical neurophysiology generations of young neurologists. During the last decade, with the transformation of “Elias” hospital neurology into a university department and re-formalizing his skills in EMG (2003) and EEG (2004), Dr. Mircea Moldovan developed his preoccupation for clinical neurophysiology teaching. Together with Dr. Ionela Codita he carries out practical demonstrations of post-graduate courses organized by Professor Dr. Panea EMG. In addition, Dr. Mircea Moldovan contributed to re-launch of the clinical neurophysiology society in Romania as founding member of ASNER 2009.

The actual neurographic examination confirmation of the sensory impairment of the left ulnar nerve and did not show significant differences with the 1984 A comprehensive diagnosis remains a challenge to this day... This presentation was determined by the wish to evaluate the historical stages of diagnostic, investigation and treatment, in homage to our colleagues from the Neurology department, and in memory of the invaluable clinical lessons of Prof. Dr.V. Voiculescu.



**Hypometabolism on PET imaging of epileptic patients – SOZ or hubs of the epileptogenic network?**

Anca Adriana Arbune

Mihai Dragos Măliia, Irina Popa, Andrei Daneasa, Csilla Nagy, Ioana Mindruta

*Spitalul Universitar de Urgenta Bucuresti, Bucuresti, Romania*

**Introduction:** Treatment resistant epilepsy is a growing problem and requires complex investigations to identify the seizure onset zone (SOZ) for the possibility of a surgical cure. PET imaging observes the metabolism of tissues, so that in epilepsy hypometabolic areas in the interictal periods appear due to increased activity during seizures and postictal glucose depletion.

**Methods:** We present the cases of three patients with treatment resistant epilepsy who underwent video-EEG long term monitoring, had MRI (epilepsy protocol), PET scan. The patients were invasively explored with depth electrodes and continuously monitored for 7-14 days. We recorded spontaneous seizures and did functional stimulations. Individual resection plans were conceived.

**Results:** We observed two males, 39 and 7 years old, and one female, 34 years old, with conflicting information from the video-EEG recordings, brain MRI and PET. The PET hypometabolism areas were located in the opposite hemisphere or at a distance from the SOZ identified by anatomo-electro-clinical correlations. SOZ surgical resections were conducted, with no postoperative deficits. Outcome of all patients is Engel I.

**Discussions:** We observed that the common characteristic of all patients was the rapid propagation from the SOZ to the structures that were correctly identified by PET imaging as hypometabolic, concluding that PET had successfully identified the main hubs of the epileptogenic network. Previous studies documented that these areas express the extent of the epileptogenic network and are correlated with seizure duration and gender.

**Conclusions:** PET imaging brings valuable information regarding the epileptogenic network but sometimes can be misleading. Epilepsy surgery should only be pursued after the anatomo-electro-clinical correlation of all information available.

**Visual evoked potentials – the influence of technical recording factors**

Mircea Moldovan

Ionela Codita, Simona Petrescu, E Georgesu, Oana Neagu, Bogdan Catalin

*Neurology Department of Elias University Emergency Hospital, Bucharest*

The visual evoked potential – VEP – represents the cerebral cortex' answer to the stimulation by light of the macular and perimacular area of the retina. The P100 latency – the constant average value – is considered a reliable indicator of clinical pathological modifications. The amplitudes of the evoked answer were associated with the axonal lesions. The presence of an asymmetry of VEP amplitude between the two eyes has determined the following observations:

**Case 1.** A 41yrs old woman, was examined for the recent diminishing of visual acuity of the left eye, through VCR thrombosis. The MRI examination revealed a compression of the optical nerve, in the supracavernous portion of ACI. On stimulation with size 8 Check, the VEP latency and amplitude was equal, normal, bilaterally. On stimulation with size 16 Check, the left eye N45 /P100 amplitude was approx. 30% smaller, and the P100/ N145 amplitude 50% smaller, in standard laboratory conditions. The P100 values of amplitude are much more sensitive in ocular and retinian lesions, than the latency values.

**Case 2.** A 55 yrs old man was first examined in December 2015 for diminished visual acuity of the left eye, onset several months earlier. The ophtalmological investigations revealed a central scotom in the eye, lowered RNFL in the temporal quadrant, macula with normal aspect; the MRI was normal. The EMG examination (without dioptric correction) has shown normal VEP morphology, an average latency of 108 ms, and the N75/P100/N145 amplitude 20% smaller in the left eye. Reexamined in 2016, the VEP parameters without dioptric correction were similar to those from 2015: the average latency P100 of 107 ms and the amplitude approx. 20% smaller in the left eye. Subsequent examination with dioptric correction of +1,25 heliomat and UV protection, presented a VEP wider [larger sau broader] in "W", with prolonged latency and slightly reduced amplitude, with pathological aspect.

**Conclusion:** The first case shows the importance of recording with different dimensions of the Check size, in order to reveal the ocular, retinal lesion. The second case demonstrates the value of dioptric correction in evidencing the pathological modifications compatible with a retrobulbar lesion of the optical nerve.

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