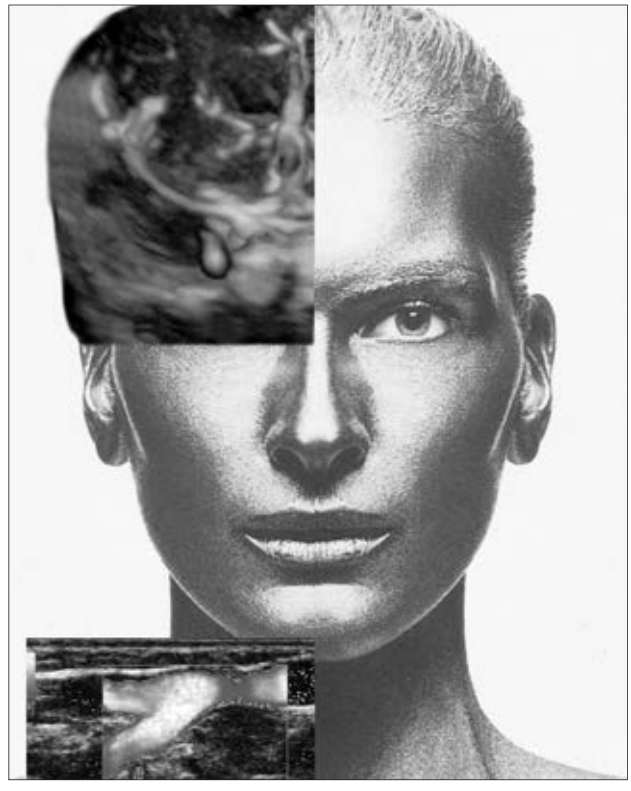
NEUROSONOLOGY AND CEREBRAL HEMODYNAMICS

НЕВРОСОНОЛОГИЯ И МОЗЪЧНА ХЕМОДИНАМИКА

Official Journal of the Bulgarian Society of Neurosonology and Cerebral Hemodynamics

Издание на Българската асоциация по невросонология и мозъчна хемодинамика



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REGIONAL TEACHING COURSE
of the European Academy of Neurology

October 6–8, 2017 | Sofia, Bulgaria

preceded by

3rd Congress of the Bulgarian Society of Neurosonology and Cerebral Hemodynamics

October 5, 2017 | Sofia, Bulgaria

Contents

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Under the Aegis

MINISTRY OF HEALTH
OF THE REPUBLIC OF BULGARIA

Министерство на
Здравеопазването

REGIONAL TEACHING COURSE
of the European Academy of Neurology

October 6–8, 2017 | Sofia, Bulgaria

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October 5, 2017 | Sofia, Bulgaria

In cooperation with

Bulgarian Society of Neurosonology and Cerebral Hemodynamics

Medical Faculty of Sofia University "St Kliment Ohridski"

Military Medical Academy – Sofia

Welcome Message

Dear Colleagues and Friends,

On behalf of the European Academy of Neurology and the Bulgarian Society of Neurosonology and Cerebral Hemodynamics we are honored to welcome you to the EAN Regional Teaching Course in Sofia from October 6th to 8th 2017. The event is in cooperation with the Medical Faculty of St Kliment Ohridski Sofia University, the Military Medical Academy – Sofia, and under the aegis of the Ministry of Health of the Republic of Bulgaria.

The EAN course is aimed at providing very high level of scientific and practical knowledge in the fields of Interventional Vascular Neurology, advance of Nonvascular Neurosonology and interdisciplinary problems such as pain and headache, autonomic dysfunction and neurorehabilitation. These topics of social importance will be presented by leading European experts.

More than 150 specialists, residents and students in Neurology, Physical Medicine, Rehabilitation, and Kinesiotherapy from Albania, Austria, Bosnia and Herzegovina, Bulgaria, Croatia, Georgia, Germany, Greece, Israel, Italy, Latvia, Macedonia, Montenegro, Poland, Portugal, Romania, Serbia, etc. have been registered for this event. Along with the training, all delegates will have the opportunity to enjoy the history and the beauty of Sofia – one of the oldest capitals in Europe.

On behalf of the Organizing Committee I wish you fruitful work!

Acad. Prof. Ekaterina Titianova
President of the Bulgarian Society
of Neurosonology and Cerebral Hemodynamics

Greeting Address

To
Acad. Prof. Ekaterina Titianova, MD, DSc
President of the
Bulgarian Society of Neurosonology
and Cerebral Hemodynamics

Dear Acad. Prof. Titianova,

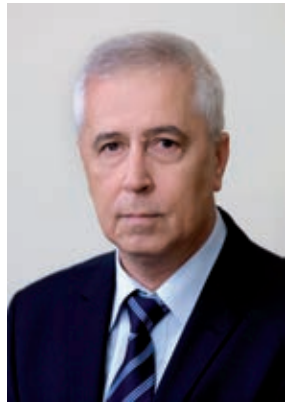
I congratulate you on the occasion of the Regional Training Course in Neurology of the European Academy of Neurology and on the occasion of the Third Congress of the Bulgarian Society of Neurosonology and Cerebral Hemodynamics.

I believe that the event will enjoy a great deal of interest in the country and abroad, and that it will help raise awareness among citizens about socially significant diseases.

Thanks to your initiative – to bring together internationally recognized and well-known specialists in the field of Neurology, Neurosonology and Cerebral Hemodynamics – the participants in the forum will exchange professional experience and knowledge about modern treatment of strokes and other neurological conditions.

I am convinced that you will contribute to the prestige of our highly humane profession and that we will thus come closer to our common goal of providing Bulgarian patients with quality and affordable healthcare at European level.

I wish you and the participants in the forum health, professional success, new scientific achievements and grateful patients.



Prof. Nikolay Petrov
Minister of Health
of the Republic of Bulgaria

Committees

Chair of the RTC
Ekaterina Titianova (Bulgaria)

RRFS – Residents and Research Fellows
Miguel Pereira

Local Organizing Committee

President
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Treasurer
E. Christova (Bulgaria)

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M. Hilz (Germany/USA)
D. Lubenova (Bulgaria)
M. Mijajlovic (Serbia)
K. Niederkorn (Austria)
L. Padua (Italy)
M. Pereira (Portugal)
F. Perren (Switzerland)
B. Stamenov (Bulgaria)
D. Staykov (Austria/Bulgaria)
E. Titianova (Bulgaria)
I. Velcheva (Bulgaria)
N. Uceyler (Germany)
U. Walter (Germany)

ean the home of neurology

БАНМХ BSNCH BULGARIAN SOCIETY OF NEUROSONOLOGY AND CEREBRAL HEMODYNAMICS

Scientific Programme

THURSDAY, 5 October 2017

3RD CONGRESS OF THE BULGARIAN SOCIETY OF NEUROSONOLOGY AND CEREBRAL HEMODYNAMICS

Hotel "Marinela"

Credits: 6 CME

3ТИ КОНГРЕС НА БЪЛГАРСКАТА АСОЦИАЦИЯ ПО НЕВРОСОНОЛОГИЯ И МОЗЪЧНА ХЕМОДИНАМИКА

Хотел „Маринела"

Кредити: 6 CME

Registration	14.00 – 18.00	**Регистрация**
General Assembly of BSNCH *(for members)*	15.30 – 16.30	**Общо събрание на БАНМХ** *(за членове)*

INNOVATIONS IN MEDICINE

ИНОВАЦИИ В МЕДИЦИНАТА

Bulgarian Society of Neurosonology and Cerebral Hemodynamics — *Българска асоциация по невросонология и мозъчна хемодинамика*

Medical Faculty of Sofia University "St Kl. Ohridski" — *Медицински факултет на Софийски университет „Св. Кл. Охридски"*

Bulgarian Academy of Sciences and Arts — *Българска академия на науките и изкуствата*

Satellite Symposium of UCB. **Active Aging by Brain Learning and Re-Learning.** *Moderator: E. Titianova*	17.00 – 17.30	**Сателитен симпозиум на UCB.** **Активно дълголетие чрез обучение и ре-обучение на мозъка.** *Модератор: Е. Титянова*
Brain Plasticity with Piracetam. *S. Andonova*		**Мозъчна пластичност с Пирацетам.** *С. Андонова*
Coffee Break	17.30 – 18.00	**Кафе пауза**
Opening Ceremony	18.00 – 18.15	**Официално откриване**
Satellite Symposium of Medtronic. **Modern Aspects of Acute Stroke Management – the Bulgarian Experience.** *Moderators: S. Andonova, N. Alioski, I. Petrov, E. Titianova*	18.15 – 19.00	**Сателитен симпозиум на Medtronic.** **Съвременни аспекти в мениджмънта на острия исхемичен мозъчен инсулт – българският опит.** *Модератори: С. Андонова, Н. Алиоски, И. Петров, Е. Титянова*
Discussion	19.00 – 19.30	**Дискусия**
Poster Session	17.00 – 20.00	**Постерна сесия**
Dinner	20.00 – 23.00	**Вечеря**

Scientific Programme

FRIDAY, 6 October 2017

REGIONAL TEACHING COURSE
of the European Academy of Neurology

Bulgarian Red Cross

Credits: 22 CME

08.00 – 18.00	**Registration**
09.00 – 09.30	**Opening Ceremony**

DAY 1:
INTERVENTIONAL VASCULAR NEUROLOGY

Chairpersons: E. Titianova (Bulgaria), K. Niederkorn (Austria)

09.30 – 10.15	**Contemporary Approach to Stroke Prevention.** *V. Demarin, S. Morović (Croatia)*
10.20 – 11.05	**Mechanical Thrombectomy in Acute Stroke.** *K. Niederkorn (Austria)*
11.05 – 11.20	**Coffee Break**
11.20 – 12.05	**The Quality of Acute Stroke Unit. A Stroke Register.** *D. Staykov (Bulgaria/Austria)*
12.05 – 12.10	Break
12.10 – 12.55	**Thrombolytic versus Standard Therapy in Acute Ischemic Stroke: A Prospective Follow up.** *S. Andonova (Bulgaria)*
12.55 – 13.00	Break
13.00 – 13.40	**RRFS – Residents and Research Fellows.** **Tips How to Start Your Career as Junior Neurologist in Europe.** *M. Pereira (Portugal)*
13.40 – 15.00	**Lunch**
15.00 – 18.00	**Interactive Workshops**
15.00 – 15.50	**The Role of Arts in Enhancement of Stroke Recovery.** *V. Demarin (Croatia)*
15.50 – 16.40	**Treatment of Intracerebral Hemorrhage – a Practical Approach.** *D. Staykov (Bulgaria/Austria)*
16.40 – 17.10	**Coffee Break**
17.10 – 18.00	**Workup of Cryptogenic Stroke.** *K. Niederkorn (Austria)*
18.30 – 22.00	**Dinner**

SATURDAY, 7 October 2017

DAY 2:
NONVASCULAR NEUROSONOLOGY UPDATE
Chairperson: Vida Demarin (Croatia), F. Perren (Switzerland)

09.00 – 09.45	**Brain Parenchyma Neurosonology.** *U. Walter (Germany)*
09.45 – 09.50	Break
09.50 – 10.35	**Ultrasound of Peripheral Nerves.** *L. Padua, C. Loreti, D. Coraci, G. Piccinini (Italy)*
10.35 – 11.00	**Coffee Break**
11.00 – 11.45	**Neuro-Orbital and Temporal Artery Ultrasound Examination.** *F. Perren (Switzerland)*
11.45 – 11.50	Break
11.50 – 12.35	**Myosonology in Neuromuscular Disorders.** *E. Titianova (Bulgaria)*
12.35 – 14.00	**Lunch**
14.00 – 17.00	**Interactive Workshops**
14.00 – 14.50	**Ultrasound in Therapeutical Management of Nerve Trauma. Hands on Nerves.** *L. Padua (Italy)*
14.50 – 15.40	**Ultrasound Imaging of Neck Muscles for Botulinum Toxin Injection.** *U. Walter (Germany)*
15.40 – 16.10	**Coffee Break**
16.10 – 17.00	**Workshop on Ultrasound. Hands on Orbita, Optic Discs and Optic Nerves.** *F. Perren (Switzerland)*
17.00 – 19.00	**City Tour**
20.00	**Gala Dinner**

SUNDAY, 8 October 2017

DAY 3:
MIXED NEUROLOGICAL ASPECTS
Chairpersons: M. Mijajlovic (Serbia), S. Andonova (Bulgaria)

09.00 – 09.45	**Guidelines on the Fibromyalgia Syndrome.** *N. Üçeyler (Germany)*
09.45 – 09.50	Break
09.50 – 10.35	**Burning Mouth Syndrome – Recent Concepts.** *M. Mijajlović (Serbia)*
10.35 – 11.00	**Coffee Break**
11.00 – 11.45	**Differential Diagnosis of Syncope and Seizure.** *M. Hilz (Germany/USA)*
11.45 – 11.50	Break
11.50 – 12.35	**Home-based Neurorehabilitation in Diabetic Neuropathy.** *D. Lubenova (Bulgaria)*
12.35 – 14.00	**Lunch**
14.00 – 15.00	**EXAM**
15.15	**Closing Ceremony** (Handout of Certificates)

TIMETABLE

Time	THU 5.10.2017	FRI 6.10.2017	SAT 7.10.2017	SUN 8.10.2017	Time
08.00–08.30		Reception desk opening	Reception desk opening	Reception desk opening	08.00–08.30
08.30–09.00					08.30–09.00
09.00–09.30		Opening Ceremony			09.00–09.30
09.30–10.00					09.30–10.00
10.00–10.30					10.00–10.30
10.30–11.00		INTERVENTIONAL VASCULAR NEUROLOGY	NONVASCULAR NEUROSONOLOGY UPDATE	MIXED NEUROLOGICAL ASPECTS	10.30–11.00
11.00–11.30					11.00–11.30
11.30–12.00					11.30–12.00
12.00–12.30					12.00–12.30
12.30–13.00		Residents and Research Fellows			12.30–13.00
13.00–13.30			Lunch	Lunch	13.00–13.30
13.30–14.00		Lunch			13.30–14.00
14.00–14.30				EXAM	14.00–14.30
14.30–15.00					14.30–15.00
15.00–15.30				Closing Ceremony (Handout of Certificates)	15.00–15.30
15.30–16.00					15.30–16.00
16.00–16.30					16.00–16.30
16.30–17.00					16.30–17.00
17.00–17.30					17.00–17.30
17.30–18.00					17.30–18.00
18.00–18.30					18.00–18.30
18.30–19.00					18.30–19.00
19.00–19.30					19.00–19.30
19.30–20.00					19.30–20.00
20.00–21.00					20.00–21.00
21.00–22.00					21.00–22.00

REGIONAL TEACHING COURSE OF THE EAN

Credits: 6 Bulgarian CME

3rd Congress of the Bulgarian Society of Neurosonology and Cerebral Hemodynamics

Reception desk opening

General Assembly of BSNCH (for members)

Satellite Symposium of UCB "Active Aging by Brain Learning and Re-Learning"

Opening

Satellite Symposium of Medtronic "Modern Aspects of Acute Stroke Management"

Poster Session

Dinner

Interactive Workshops

Dinner
Free time

Interactive Workshops

City Tour

Gala Dinner

RTC EAN Credits: 22 CME

Bulgarian Medical Association

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БАНМХ BSNCH BULGARIAN SOCIETY OF NEUROSONOLOGY AND CEREBRAL HEMODYNAMICS

REGIONAL TEACHING COURSE
of the European Academy of Neurology

October 6–8, 2017 | Sofia, Bulgaria

LECTURERS

Prof. Vida Demarin, MD

Education: Professor Vida Demarin, MD, Ph.D. graduated from School of Medicine, University of Zagreb, Croatia, where she gained her Master of Science thesis and Doctor of Philosophy degree. She finished her residency in Neuropsychiatry in Sestre milosrdnice University Hospital Centre, Zagreb, Croatia.

She was Head of Department of Clinical Neurology and Centre for Neurological Sciences and Brain Research in University Hospital Centre "Sestre Milosrdnice" from May 1994 until November 2011. Under her leadership the Department became Reference Centre for Neurovascular Disorders and Reference Centre for Headaches of Ministry of Health of Republic of Croatia. From November 2011 until September 2012, she was Counselor for International Collaboration in the same institution. She was Medical director of Medical Centre Aviva from September 2012 until December 2015, when she became a president of International Institute for Brain Health.

She is a full member and fellow of Croatian Academy of Sciences and Arts. She published more than 1000 papers in national and international journals, organized and participated in numerous symposia, seminars, conferences and congresses. She mentored numerous Doctor of Philosophy and Master of Science theses, research fellows, residents and students.

Research fields: stroke prevention and management, neurorehabilitation, neurodegenerative disorders and dementia, management of headache and migraine, neuroplasticity, and neuropathic pain. She was principal investigator of numerous research projects. She is a pioneer of neurosonology in Croatia, and the founder of Summer Stroke School – Healthy Lifestyle and Prevention of Stroke and Brain Impairment, that has been organized in Dubrovnik, Croatia since 1990.

She was president of Croatian Neurological Society during two terms and she organized first national neurological congress. She was founder and the first president of Croatian Society for Neurovascular Disorders and Croatian Stroke Society, whose workgroup published national Recommendations for Stroke Management 2001 and 2006, as well as Evidence based Guidelines for Management of Primary Headaches 2005 and 2008, Consensus Opinion on Brain Death Diagnosing 2005, and Recommendations for the Management of Patients with Carotid Stenosis 2010. She initiated national program of stroke management, organization of stroke unit network and thrombolysis therapy in Croatia. For several decades she leads and organizes national stroke and cerebrovascular disease prevention programs, educating citizens, general practitioners and neurologists. All her projects are devoted to raising health awareness and improving the quality of life. She authored numerous publications dedicated to lifestyle improvement and disease prevention.

Memberships: Member of numerous national and international professional societies, president of Kuratorium of Mind&Brain International Neuropsychiatric Pula Congresses, and president of Central and Eastern European Stroke Society and the Secretary General of the WFN Applied Research Group on Organization and Delivery of Care. She is member of the Executive Board of the Academy of Medical Sciences of Croatia, Fellow of American Academy of Neurology, Fellow of American Heart Association, Fellow of European Stroke Organization, Fellow of European Academy of Neurology, member of World Stroke Organization Board of Directors and member of WSO Education Committee, as well as a member of International Headache Society, EAN Scientific Panel for Stroke, EAN Scientific Panel for Headache, EAN Scientific Panel for Neurosonology and EAN Scientific Panel on Higher Cortical Functions, Vice President of Croatian Brain Council, and more.

She developed intensive collaboration with colleagues from all over the world and especially with colleagues from central and eastern European countries, in order to spread knowledge and skills and interchange of ideas among all of us. She participated as a lecturer at several ESO Summer Schools as well as at several RTCs, building new connections and friendships. Only working together, under WFN motto: *There is no health, without brain health*, we can be successful in the fight against brain diseases.

Prof. Kurt Niederkorn, MD

Education: Medical School Graz, Austria (1973 – 1980); Residency, University Dep. of Neurology, Graz, Austria (Since 1980).

Career Experience: Faculty Member, University Dep. of Neurology, Graz (since 1988);Assistant Prof. of Neurology (1989); Asssociate Prof. of Neurology; Chief, Section of Neurosonology (1991); Professor of Neurology (1996); Vice Chairman, Dep. of Neurology Graz (1996 – 2013); Deputy Head, Section of General Neurology (2005 – at present); Head, Stroke Unit,Stroke outpatient clinic and Neurology Emergency Service Dep. of Neurology Graz (2001 – at present).

Publications: More than 220 publications; Reviewer for Stroke, Cerebrovascular Diseases, Journal of the Neurological Sciences, Journal of Neuroimaging, European Journal of Ultrasound, etc.

Memberships: European Society of Neurosonology and Hemodynamics (President 2005-2009); Neurosonology Research Group of the World Federation of Neurology (Executive Committee Member until 2009); American Academy of Neurology; American Society of Neuroimaging; Austrian Society of Neurology; Honorary member, Bulgarian Society of Neurosonology and Cerebral Hemodynamics.

Local PI: ECASS 2, 3 and 4; SPACE and SPACE2, Chrystal-AF, Endostroke, Austrian Stroke Registry, Swift-Prime.

Priv.-Doz.
Dimitre Staykov, MD

Education: Priv.-Doz. Dr. Staykov has graduated from the University of Vienna, Austria and recieved his training in neurology, neurocritical care and gerontology at the University Hospital Erlangen, Germany.

Career Experience: Since April 2015 Dr. Staykov chairs the Department of Neurology at the Hospital of the Brothers of St. John Eisenstadt, Austria.

Research fields: Priv.-Doz. Dr. Staykov's recent research is related to the treatment of intraventricular hemorrhage, the development of imaging analysis techniques and quantification of perihemorrhagic brain edema, and therapeutic hypothermia in ischemic and hemorrhagic stroke.

Publications: Priv.-Doz. Dr. Staykov has published more than 50 peer-reviewed articles in international scientific journals and has co-authored guidelines of the Neurocritical Care Society, the European Stroke Organization and the German Neurological Society.

Miguel António
Tábuas-Pereira, RRFS

Education: High School from the Escola Secundária Francisco Rodrigues Lobo – Leiria (2005); Medicine Masters Degree in the Faculdade de Medicina da Universidade de Coimbra (2011).

Career Experience: Neurology residency program at the Neurology Department – Centro Hospitalar e Universitário de Coimbra (since 2013); General residency program at the Centro Hospitalar e Universitário de Coimbra (2012).

Publications: autor and co-author of 7 publications and 24 presentations in scientific events.

Memberships: Since 2016 he is a RRSF member of the Education Committee of the European Academy of Neurology and member of the EAN Higher Cortical Functions Scientific Panel.

Assoc. Prof.
Uwe Walter, MD

Education: Medical School Graz, Austria (1973 – 1980); Residency, University Department of Neurology, Graz, Austria (Since 1980).

Career Experience: Faculty Member, University Department of Neurology, Graz (since 1988); Assistant Prof. of Neurology (1989); Associate Prof. of Neurology; Chief, Section of Neurosonology (1991); Professor of Neurology (1996); Vice Chairman, Dep. of Neurology Graz (1996–2013); Deputy Head, Section of General Neurology (2005 – at present); Head, Stroke Unit, Stroke outpatient Clinic and Neurology Emergency Service Dep. of Neurology Graz (2001 – at present).

Publications: More than 220 publications; Reviewer for Stroke, Cerebrovascular Diseases, Journal of the Neurological Sciences, Journal of Neuroimaging, European Journal of Ultrasound, etc.

Memberships: European Society of Neurosonology and Hemodynamics (President 2005–2009); Neurosonology Research Group of the World Federation of Neurology (Executive Committee Member until 2009); American Academy of Neurology; American Society of Neuroimaging; Austrian Society of Neurology; Honorary member, Bulgarian Society of Neurosonology and Cerebral Hemodynamics.

Local PI: ECASS 2, 3 and 4; SPACE and SPACE2, Chrystal-AF, Endostroke, Austrian Stroke Registry¸ Swift-Prime.

Assoc. Prof.
Luca Padua, MD

Education: Dr. Padua has graduated from the "La Sapienza" University, Rome in 1986. He obtained specialty of Neurology in 1990 at the Università Cattolica del Sacro Cuore, Rome. He received PhD degree at the Università Cattolica del Sacro Cuore, Rome in 1996.

Career Experience: Researcher in the Department of Neuroscience, Institute of Neurology Università Cattolica del Sacro Cuore Rome (2001–2015); Scientific Referee of the Roman Centres of Don Gnocchi Foundation Onlus (since 2005); Director of Physical Therapy Board (since 2015); Associated Professor of Department Geriatrics, Neurosciences and Orthopaedics at the Università Cattolica del Sacro Cuore, Policlinico Agostino Gemelli – Rome (since 2015).

Research fields: ultrasound of peripheral nerves, neurorehabilitation, multicenter studies in Charcot-Marie-Tooth Disease, Fabry Disease, neurogenetics.

Memberships: Member of the Board of Directors of the SINC (Società Italiana di Neurofisiologia Clinca), Member of the Board of Directors of the ASNP (Associazione Italiana per lo Studio del Sistem nervosa Periferico).

Prof. Fabienne Perren, MD

Education: Doctoral thesis in medicine: University of Lausanne, Switzerland; Swiss federal Diploma of Medicine, University of Lausanne, Switzerland; Swiss specialty board certificate in cerebrovascular diseases, Swiss Society of Clinical Neurophysiology FMH (2004); Swiss specialty board certificate in Neurology Swiss Society of Neurology FMH (2005); Certificate of management for senior doctors of the University Hospital of Geneva HUG (2007); International Certificate in Neurosonology ESNCH (2008); Privat Docent Thesis "Transcranial ultrasound in stroke and its new developments" Medical Faculty University of Geneva (2009); Professor of Neurology of the Faculty of Medicine in Geneva, Switzerland (2016).

Career Experience: Resident in Internal Medicine, Hospital of Nyon, Switzerland (1998–1999); Resident in Neurology, Department of Neurology, CHUV, University Hospital of Lausanne, Switzerland (1999–2002); Clinical and Research Fellow, Neurosonology & Cerebrovascular Units, Department of Neurology, University Hospital Mannheim, University of Heidelberg, Mannheim, Germany (2002–2004); Member of the European research project group UMEDS: Ultrasonographic Monitoring and Early Diagnosis of Stroke (2003–2004); Instructor (Cheffe de clinique), Department of Neurology, HUG, University Hospital, Geneva, Switzerland (2004–2007); Instructor (Cheffe de clinique), Departments of Neurology, Interventional Neuroradiology and Neurosurgery, HUG, University Hospital, Geneva (2007–2008); Attending (Médecin adjointe), Department of Neurology, HUG, University Hospital, Geneva (since 2008); Attending Neurovascular and Neurosonology Unit, Dept of Neurology, HUG, University Hospital, Geneva (since 2009).

Membership: Member of the American Academy of Neurology, European Society of Neurosonology and Cerebral Hemodynamics, Swiss Neuroscience Society Swiss Neurological Society, Swiss Society of Neurophysiology International Stroke Society Swiss Cerebrovascular Task Force/ZAS, Executive Committee Member and Treasurer of the Neurosonology Research Group of the World Federation of Neurology (since 2009), Member of the editorial board of "Neurosonology" (since 2010), Member of the editorial board of "BMC Neurology", Fellow of the ESO – European Stroke Organisation.

Prof. Nurcan Üçeyler, MD

Education: Prof. Üçeyler studied Medicine at the Medical School of the University of Würzburg, Germany and received her medical licence in 2002. 1999–2003 she completed her doctoral thesis at the Department of Internal Medicine of the University of Würzburg and started her professional career at the Department of Neurology, University of Würzburg in 2003. In 2008 she received her licence for Neurophysiology and spent three months as guest scientist at Yale University, Neuroscience and Regeneration Research Center, New Haven, USA (Prof. S. Waxman). In 2009 Prof. Üçeyler received her board certification as Neurologist and in 2014 as Pain Specialist. In 2010 she completed her "Habilitation" for Neurology (i.e. German qualification for professorship) and became Professor of Neurology in 2016.

Research fields: Since 2003 Dr. Üçeyler is continuously performing clinical and animal studies on the pathophysiology of neuropathic pain, generalized pain disorders, and peripheral neuropathies – particularly small fiber neuropathies. She serves as a peer reviewer for several scientific journals and is an Academic Editor of PlosOne.

Awards: In 2010 she won the EFIC Grünenthal award and in 2014 the award of the Sertürner-Society for outstanding pain research.

Ass. Prof. Milija D. Mijajlovic, MD

Education and Carrier: Ass. Prof. M. Mijajlovic, MD, PhD is Ass. Professor of Neurology at School of Medicine University of Belgrade, Serbia. He is working as Board Certified Neurology Specialist, Neuroangiology expert and Head of the Neurosonology Unit at the Department for Cerebrovascular Disorders of the Neurology Clinic, Clinical Center of Serbia in Belgrade. Dr. Mijajlovic is a Research Associate of the Ministry of Science and Education of Serbia. He received his Masters Degree in Neurology (Stroke) and PhD title in Neurology from School of Medicine University of Belgrade. He was trained at the Department of Neurology University of Muenster, at Neurology Clinic of the TU Dresden, at Stroke Unit of the Sackler Medical Center, Tel Aviv University, at Stroke Unit of the Vall d'Hebron Hospital in Barcelona, at the Neurology Department of the University hospital in Amines in France and Hertie Institute for clinical brain research in Tuebingen, Germany.

Research fields: His research is focused on stroke, neuroangiology, neurosonology, neurodegenerative diseases and headaches/pain.

Memberships: Ass. Prof. M. Mijajlovic is a member of the Executive Committee of the Neurosonology Research Group of the World Federation of Neurology, the Neurosonology and Stroke Subspecialist Panels of the European Academy of Neurology, and the Teaching course Committee of the European Academy of Neurology. He is a Senior Editor of the Clinical Case Reports Journal, member of the Editorial Board of the Journal of Ultrasound in Medicine (from which he received distinguished reviewer award in 2014), and a Guest Editor of the Journal of Neurosonology and Cerebral Hemidynamics. He serves as invited reviewer for more than 20 peer reviewed journals. He is author of more than 100 articles published in peer-reviewed journals, invited speaker at more than 50 international and local conferences, and coauthor of 18 books and book chapters.

Prof. Max J. Hilz, MD

Education: Prof. Dr. med. Dr.med.habil. Max J. Hilz studied medicine at the Universities of Cologne and Erlangen-Nuremberg in Germany. After he had defended his doctoral thesis in 1980, he trained in Anesthesiology and Intensive Care Medicine and in Ear-Nose-and–Throat diseases (1980–1982). He started his residency in Neurology and Psychiatry at the University of Erlangen-Nuremberg. He specialized in Neurology, Clinical Neurophysiology, Neurological Intensive Care Medicine and Disorders of the Autonomic Nervous System (ANS), and holds German board certificates in Neurology and Psychiatry and in Psychotherapy. He also passed the board examination of the American Board of Electrodiagnostic Medicine. He is licensed to practice medicine in Germany, the United Kingdom, and in the State of New York, USA.

Career Experience: Since June 2015, he is Professor of Neurology at the University of Erlangen-Nuremberg in Erlangen, Germany. He is also Adjunct Professor of Neurology at Icahn School of Medicine at Mount Sinai, New York, NY, USA. Form September 1, 2016 to August 31, 2017, he was the Chair in Autonomic Neurology, and Director of the Clinical Department of Autonomic Neurology at the University College London, Institute of Neurology, Queen Square, London, UK. He was Professor of Neurology in Medicine and Psychiatry at the New York University, New York, NY (1992–2013). He also served as the Associate Director of the NYU Dysautonomia Evaluation and Treatment Center (until 2007). He was deeply involved in clinical research regarding the pathophysiology of Familial Dysautonomia, also known as Riley-Day syndrome or Hereditary Sensory and Autonomic Neuropathy Type III, and in studies of Fabry disease that led to the approval of enzyme replacement therapy in the USA.

Research fields: Prof. Hilz is experienced in the examination of small nerve fiber diseases and disorders of the autonomic nervous system, including hereditary sensory and autonomic neuropathies, diabetic neuropathies, and Fabry disease, and central autonomic disorders. He also served as an advisor to the European Medicines Agency, EMA, on issues related to autonomic nervous system dysfunction.

Memberships: Professor Hilz is a member of 16 national and international scientific societies and is on the board of several autonomic nervous system societies. He currently co-chairs the Autonomic Nervous System Subspecialty Panel of the European Academy of Neurology, EAN. He also is Past-President of the German Autonomic Society, Past-President of the European Federation of Autonomic Societies, and Past-Chair of the Autonomic Section of the American Academy of Neurology. He is ad hoc reviewer for more than 25 international scientific journals, a member of the editorial board of Clinical Autonomic Research, and Associate Clinical Editor of Autonomic Neuroscience: Basic and Clinical. He co-authored the guidelines of the German Neurological Society on syncope, the guidelines on erectile dysfunction and the guidelines of the German Diabetes Society on diabetic neuropathy. He has published more than 300 original and review articles in peer-reviewed journals and chapters in textbooks and presented his work at several hundred scientific conferences.

Acad. Prof. Ekaterina Titianova, MD

Education: Acad. Titianova graduated from the Medical Academy – Sofia in 1982. In 1997 she acquired specialty in Neurology, in 1990 became PhD, and in 2007 – Doctor of Sciences (DSc). She has specialized in Neurology, Neurosonology, gait motor control, and Neurorehabilitation at prestigious universities in Austria, USA, Mexico, Germany, and Finland. In 2003 she became an Associate Professor, and in 2009 – Professor of Neurology.

Current positions: At present she is Professor of Neurology, Head of the Clinic of Functional Diagnostics of Nervous System at the Military Medical Academy, Sofia, member of the Faculty Council and Head of the Department of Neurology, Psychiatry, Physiotherapy and Rehabilitation, Preventive Medicine and Public Health at the Medical Faculty of St Kliment Ohridski Sofia University. Since 2013 she has been Academician of the Bulgarian Academy of Sciences and Arts and since 2015 – Academician of the Serbian Royal Academy. She is an expert at the Ministry of Health, the National Agency for Assessment and Accreditation at the Council of Ministers, and the National Health Insurance Fund of the Republic of Bulgaria. She is also an expert of the European Commission of the European Union.

Scientific activities: Her scientific works include monographs, textbooks, manuals and more than 250 publications. She works as PI, national coordinator or contributor to a number of international trials. She has been a visiting lecturer and chairperson of many scientific events.

Research fields: cerebrovascular disease, neurosonology, cerebral hemodynamics, hemorheology, autonomic failure, orthostatic intolerance, gait motor control, neurorehabilitation.

Memberships: Acad. Titianova is founder and President of the Bulgarian Society of Neurosonology and Cerebral Hemodynamics (since 2005), Member of the Executive Committee of the WFN Neurosonology Research Group (since 2009). For many years now she has been the Bulgarian coordinator of the CME programmes of the World Federation of Neurology. She is the editor-in-chief of the English-Bulgarian Journal of Neurosonology and Cerebral Hemodynamics, and also member of the editorial boards of international scientific journals of Neurosonology (Japan), Archivos de Neurociencias (Mexico), and Oruen.

Awards: Merrill Spencer Award 2009, Golden Hyppocratic Oath of the Balkan Association for History and Philosophy of Medicine, Honorary Plaque of the Bulgarian Ministry of Defense, and a number of best poster prizes.

Prof. Silva Andonova, MD

Education: High School Degree (1989); Degree in Medicine (1996); Degree in Healthcare Management (2015); Specializations: Neurology (2004); Post-graduate training: Neurosonology – Medical University – Sofia (2003, 2006), Military Medical Academy (2007, 2008), Qualification Course for Accreditation Experts of the European Quality Management Fund EFQM, Zurich, Switzerland (2007, 2015).

Career Experience: neurologist in an emergency room MHAT "St Anna", Varna, assistant at the Department on Neurological Sciences, Medical University of Varna, Bulgaria (2003–2012); Assistant professor at the Department on Neurological Sciences, Medical University of Varna, Bulgaria (2012–2016); Professor at the Department on Neurological Sciences, Medical University of Varna, Bulgaria (since 2016); Head of Second clinic of neurology with Intensive Care Unit and Stroke Unit – University Hospital "St Marina" – Varna (since 2009); Director of Medical Diagnostic Activity – University Hospital "St Marina" – Varna, Bulgaria (since 2017).

Teaching: Neurology for students in the specialty "Medicine" – University of Varna, Bulgaria (since 2003); Neurology for students in the specialty "nurses" – University of Varna, Bulgaria (2006–2013); Neurology for students in the specialty "Social activities" – University of Varna, Bulgaria (2007–2008); lector and coordinator of teaching course in Neurosonology – Univesrity of Varna (since 2010).

Publications: autor and co-author of more than 150 publications in national and international Journals.

Membership: Member of the Executive Committee of Bulgarian Society of Neurosonology and Cerebral Hemodynamics (since 2015), Member of the European Stroke Organisation (since 2014), Member of the Editorial Advisory Board of Bulgarian Journal "Neurosonology and Cerebral Hemodynamics" (since 2015).

Prof. Daniela Lubenova, PhD

Current positions: Prof. Daniela Lubenova, PhD is a Professor of Kinesiotherapy. Head of Department "Kinesiotherapy and Rehabilitation" and Vice Dean of the "Vasil Levski" National Sports Academy. Head of the Master's programs "Kinesiotherapy" and "Physical therapy and rehabilitation" in National Sports Academy. She is expert at the National Agency for Assessment and Accreditation at the Council of Ministers.

She has specialized in Kinesiotherapy at prestigious universities in Hungary, Finland, England and Norway. Her research fields are focused on neurorehabilitation, proprioceptive neuromuscular facilitation, methodology Perfeti, kinesioteyping, methods of Bobath, cardiological and pulmonary rehabilitation.

Carieer Experience: Rehabilitator in clinic "Physiotherapy and rehabilitation", III City United Hospital – Sofia (1988–1995); assistant at the Department "Kinesiotherapy and Rehabilitation", "Vasil Levski" National Sports Academy – Sofia (1995–2009); Associate professor at the Department "Kinesiotherapy and Rehabilitation", "Vasil Levski" National Sports Academy – Sofia (2009–2016); Professor at the Department "Kinesiotherapy and Rehabilitation", "Vasil Levski" National Sports Academy – Sofia (since 2016).

Teaching: Kinesiotherapy in neurological and psychiatric diseases, kinesiotherapy in internal medicine, kinesiotherapy in geriatrics for students in the specialty "Kinesiotherapy", Bachelor's degree in "Vasil Levski" National Sports Academy – Sofia; Neurorehabilitation for students in the specialization to the Master's program "Kinesiotherapy" and "Physical therapy and rehabilitation".

Scientific activities: Prof. Lubenova is author and co-autor of more than 80 publication, including 5 books and 3 monographs. She has participated in the governing body of scientific projects at international level and in more than 50 congresses at home and abroad.

Scientific Societies: Prof. Lubenova is a member of the Association of Physiotherapist in Bulgaria, an associated of the Bulgarian Association of Neurosonology and Cerebral Hemodynamics and member of the editiorial board of the Journal "Kinesiotherapy". She is a member of the World Confederation for Physical Therapy and European Network of Physiotherapy in Higher Education.

Research fields: kinesiotherapy, neurorehabilitation, gait, stroke, diabetic neuropathy, cardiologic and pulmonary rehabilitation, ets.

Contemporary Approach to Stroke Prevention

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Key words:
Mediterranean diet, physical activity, risk factors for stroke, stroke, stroke prevention

Stroke is a heterogenous and multifactorial disease caused by the combination of vascular risk factors, environment and genetic risk factors. It is defined by WHO (World Health Organization) as the clinical syndrome of rapid onset of focal or global cerebral deficit, lasting more than 24 hours or leading to death, with no apparent cause other than a vascular one. It is one of the most common causes of death and disability in the adult population of the modern society. Stroke is a life changing disease, affecting the quality of life of patients and their families. It is also a huge social and financial burden for the family as well as the society. In spite of huge development in the management of stroke, with stroke units, thrombolytic therapy, endovascular treatment, neurosurgical and vascular surgical treatment, primary prevention of stroke is still one of the most important contributors for stroke management. Stroke risk factors can be subdivided into non-modifiable (age, sex, race-ethnicity, genetic factors) and modifiable (hypertension, diabetes, dyslipidemia, atrial fibrillation, carotid artery stenosis, smoking, poor diet, physical inactivity, and obesity). The four most important keys for healthy brain are in our hands: healthy nutrition (Mediterranean Diet), regular physical activity, stress management and "brain fitness".

Brain diseases are frequent, causing disability and changes in the quality of life of the patients and their families, as well as having a huge social and financial burden. According to European Brain Council costs of brain disorders in Europe are 798 billions of Euros per year, what is one third of the whole health expenditure per year, with stroke contributing a great deal to this situation.

Adequate blood supply of the brain is prerequisite for brain health with control and management of behavioral, enviromental and metabolic risk factors. In spite of huge development in the management of stroke, with stroke units, thrombolytic therapy, endovascular treatment, neurosurgical and vascular surgical treatment, primary prevention of stroke is still one of the most important contributors to the brain health.

Obviously, over the years, we missed to fill out several gaps in stroke prevention. Despite efforts to modify health behavior, the knowledge about stroke, it's risk factors and symptoms is low, which means there is still lack of awareness. Then, "low risk" individuals are falsly reassured and therefore are not motivated. The management of hypertension is not properly addressed. Important risk factors for stroke are not considered in sreening (i.e. sedentary lifstyle, alcohol intake). The specificity of cerebovascular disease (CVD) prediction algorithms is low due to the fact they may not be applicable to all races. There is also a cost barrier for some high risk strategies, lack of effectiveness in screening of high-risk inividuals and not implementation of some already created population-wide strategies [10, 23].

The four most important keys for healthy brain are in our hands: healthy nutrition (Mediterranean Diet), regular physical activity, stress management and "brain fitness".

The importance of nutrition in preserving the brain health is a subject of investigation for many years, pointing out the role of polyunsaturated fatty acids from fish consumtion, abundance of fruits and vegetables, whole grains, olive oil and red wine, what are all main ingredients of Mediterranean Diet. The adherence to this diet leeds to improved endothelial function, increased plasma antioxidant capacity and reduction of insulin resistence, what contributes to prevention of stroke, neurodegenerative disorders, metabolic syndrome, etc.

Regular physical activity increases the level of BDNF that is of utmost importance for cognitive functioning and decreased risk of depression and stroke.

Control and management of stress in a daily living is the third key in preserving healthy brain especially important nowdays when human circuits are overloaded and people are bombarded with constantly changing mental challenges. It is estimated that we encounter a thousand times more events per year than our great-grandparents did, but the time available for decision-making remains the same or even less. In the era of person-centered approach, techniques for stress

relieve should be individually tailored and stress should be properly managed.

And the fourth key, again something what we can practice by ourselves is an array of different brain fitness tasks which challenge our brain and contribute greatly to healthy brain.

In this article we will look more closely at two of several keys to preserving brain health: benefits of Mediterranean diet and physical exercise.

Primary prevention of stroke by healthy nutrition

The combination of healthy lifestyle factors is associated with lower risk of coronary heart disease, diabetes, and total cardiovascular disease. A prospective cohort study [3] among 43 685 men from the Health Professionals Follow-up Study and 71 243 women from the Nurses' Health Study evaluated diet and other lifestyle factors. Low-risk lifestyle was defined as: not smoking, a body mass index <25 kg/m^2, >30 min/d of moderate activity, modest alcohol consumption (men, 5-30 g/d; women, 5-15 g/d), and scoring within the top 40% of a healthy diet score. There were 1559 strokes (853 ischemic, 278 hemorrhagic) among women and 994 strokes (600 ischemic, 161 hemorrhagic) among men during follow-up. Women with all 5 low-risk factors had a relative risk of 0.21 (95% CI, 0.12, 0.36) for total and 0.19 (95% CI, 0.09, 0.40) for ischemic stroke compared with women who had none of these factors. Among men, the relative risks were 0.31 (95% CI, 0.19, 0.53) for total and 0.20 (95% CI, 0.10, 0.42) for ischemic stroke for the same comparison. Among the women, 47% (95% CI, 18 to 69) of total and 54% (95% CI, 15 to 78%) of ischemic stroke cases were attributable to lack of adherence to a low-risk lifestyle; among the men, 35% (95% CI, 7 to 58) of total and 52% (95% CI, 19 to 75) of ischemic stroke may have been prevented. A low-risk lifestyle, associated with a reduced risk of multiple chronic diseases also may be beneficial in the prevention of stroke, especially ischemic stroke. Consumption of plant foods and dairy and meat products may moderate increases in blood pressure. Association of dietary intake with 15-y incidence of elevated blood pressure was evaluated in the Coronary Artery Risk Development in Young Adults (CARDIA) Study (26) of 4304 participants. Plant food intake (whole grains, refined grains, fruit, vegetables, nuts or legumes) was inversely related to elevated blood pressure (EBP) after adjustment for age, sex, race, center, energy intake, cardiovascular disease risk factors, and other potential confounding factors. Compared with quintile 1, the relative hazards of EBP for quintiles 2–5 of plant food intake were 0.83 (95% CI: 0.68, 1.01), 0.83 (0.67, 1.02), 0.82 (0.65, 1.03), and 0.64 (0.53, 0.90). Dairy intake was not related to EBP, and positive dose-response relations for EBP were observed across increasing quintiles of meat intake. In subgroup analyses, risk of EBP was positively associated with red and processed meat intake, and inversely associated with intakes of whole grain, fruit, nuts, and milk. These findings are consistent with a beneficial effect of plant food intake and an adverse effect of meat intake on blood pressure. Increased consumption of fruit and vegetables has been shown to be associated with a reduced risk of stroke in most epidemiological studies, although the extent of the association is uncertain. Meta-analysis of cohort studies [14] quantitatively assessed the relation between fruit and vegetable intake and incidence of stroke. Groups included 257 551 individuals (4917 stroke events) with an average follow-up of 13 years. Compared with individuals who had less than three servings of fruit and vegetables per day, the pooled relative risk of stroke was 0.89 (95% CI 0.83–0.97) for those with three to five servings per day, and 0.74 (0.69–0.79) for those with more than five servings per day. Subgroup analyses showed that fruit and vegetables had a significant protective effect on both ischaemic and haemorrhagic stroke. Increased fruit and vegetable intake in the range commonly consumed is associated with a reduced risk of stroke. Results provide strong support for the recommendations to consume more than five servings of fruit and vegetables per day, which is likely to cause a major reduction in strokes.

Mediterranean diet

Meta-analysis of 12 studies (25) (n=1574299) evaluating the association of the adherence to a Mediterranean diet and the mortality and incidence of major cardiovascular diseases (CVD) and chronic neurodegenerative diseases showed that the greater adherence to a Mediterranean diet was associated with significant reduction in overall mortality (9%), mortality from CVD (9%), incidence of or mortality from cancer (6%), and incidence of Parkinson's disease and Alzheimer's disease (13%) [25]. Mediterranean Diet and Incidence and Mortality from Coronary Heart Disease and Stroke in Women study [12] was performed in 4886 women, with no history of cardiovascular disease and diabetes (Nurses' Health Study) and followed up. Alternate Mediterranean Diet Score (aMED), focusing on higher consumption of plant foods, including plant proteins, monounsaturated fat, fish and lower consumption of animal products and saturated fat ranged from 0 to 9, with a higher score representing closer resemblance to the

Mediterranean diet. Results demonstrated 2391 incident cases of CHD (1597-nonfatal and 794-fatal), 1763 incident cases of stroke (959 ischemic, 329 hemorrhagic and 475 unclassified). Of all strokes, 1480 cases were nonfatal and 283 cases were fatal. There were 1077 cardiovascular disease deaths (fatal CHD and strokes combined) [15]. Long-chain ω-3 polyunsaturated fatty acids (LCn3PUFAs): eicosapentaenoic acids (EPA), docosapentaenoic acid (DPA), docosahexaenoic acid (DHA) in fish are the key nutrients responsible for the cardio-protective benefits and CVD prevention. Beneficial effects of fish consumption on the risk of CVD are derived from synergistic effects among nutrients in fish. Fish is considered to be an excellent source of proteins with low saturated fat (taurine, arginine, glutamine-known to regulate cardiovascular function)' and some nutritious trace elements (selenium and calcium) which may directly or indirectly provide cardiovascular benefits, alone or in combination with LCn3PUFAs and vitamins (vitamin D and B). Interactions between LCn3PUFAs and other nutrients, including nutritious trace elements and vitamins and amino acids are important in reducing the risk of CVD. Overall favorable effect is observed on: lipid profiles, threshold for arrhythmias, platelet activity, inflammation and endothelial function, atherosclerosis and hypertension. The American Heart Association recommends eating fish (particularly fatty fish) at least 2 times a week. Fish consumption may be inversely associated with ischemic stroke but not with hemorrhagic stroke, because of the potential antiplatelet aggregation property of LCn3PUFAs. A meta-analysis of 8 independent prospective cohort studies which included 200575 subjects and 3491 stroke events showed that individuals with higher fish intake had lower risk of total stroke, compared with those who never consumed fish or ate fish less than once per month. The reduction in risk of total stroke was statistically significant for fish intake once per week; for individuals who ate fish 5 times or more per week, the risk of stroke was lowered by 31%. The risk of ischemic stroke was also significantly reduced by eating fish twice per month. It has been suggested that broiled and baked fish, but not fried fish and fish sandwiches, are associated with a lower incidence of atrial fibrillation (AF) and ischemic heart disease. Cardiovascular Health Study [27] evaluated 3660 subjects aged over 65 who underwent an MRI scan to associate fish consumption and risk of subclinical brain abnormalities on MRI in older adults. Among older adults, modest consumption of tuna/other fish, but not fried fish, was associated with lower prevalence of subclinical infarcts and white matter abnormalities on MRI examinations. Tuna or other fish consumption was also associated with trends toward lower incidence of subclinical infarcts and with better white matter grade. No significant associations were found between fried fish consumption and any subclinical brain abnormalities. After adjustment for multiple risk factors, the risk of having one or more prevalent subclinical infarcts was lower among those consuming tuna or other fish ≥3 times per week, compared to <1 per month. The risk reduction (RR) in those consuming tuna/other fish ≥3 times per week was 0.56 compared to <1 per month. Each one serving/week of tuna/other fish was associated with trends toward 11% lower RR of any incident subclinical infarct and 12% lower RR of each additional multiple infarct. Consumption of omega-3 fatty acids is not associated with a reduction in carotid atherosclerosis according to the Genetics of Coronary Artery Disease in Alaska Natives Study [7]. The study included population-based sample that underwent ultrasound assessment of carotid atherosclerosis. Intima-media thickness (IMT) of the far wall of the distal common carotid arteries and plaque score (number of segments containing plaque) were assessed. Mean consumption of total omega-3 FAs was 4. 6 g/day in those without and 5.07 g/day in those with plaque. Presence and extent of plaque were unrelated to intake of C20–22 omega-3 fatty acids (FAs) or total omega-3 FAs. The odds of plaque rose significantly with quartiles of palmitic and stearic acid intake. The extent of plaque (or plaque score) was also associated with a higher percentage intake of palmitic acid. IMT was negatively associated with grams of C20–22 omega-3 FAs, total omega-3, palmitate, and stearate consumed. Dietary intake of omega-3 FAs in a moderate-to-high range does not appear to be associated with reduced plaque, but is negatively associated with IMT. The presence and extent of carotid atherosclerosis among Eskimos is higher with increasing consumption of saturated FAs. No significant differences were seen in the prevalence of atherosclerotic plaque or mean plaque score with increasing quartiles of dietary intake of either total omega-3 FAs or C20–22 omega-3 FAs. When analyzed as percentage of total fat intake, C20–22 consumption and total omega-3 FA consumption were not related to average IMT. When the analyses were adjusted for age and gender, positive associations were observed between the percentage of fat intake from palmitic or stearic acid and the presence of plaque and plaque score. When analyzed as daily intake in grams, higher quartiles of intake of either palmitate or stearate were associated with significantly higher average IMT, when adjusted for age and gender [7].

The randomized, multicenter trial of Mediterranean diet in primary prevention of cardiovascular events in Spain, randomly

assigned participants who were at hight CV risk to one of three diets: Mediterranean diet supplemented with extra-virgin olive oil, the other one supplemented with mixed nuts, or a control diet (adviced to reduce dietary fat), included 7447 persons (aged 55-80 years), followed up during 4,8 years. Mediterranean diet with extra-virgin olive oil and the one supplemented with nuts, reduced the incidence of major CV events [9].

Tea consumption and risk of stroke

A meta-analysis of green and black tea consumption and risk of stroke [1] included data from 9 studies involving 4378 strokes among 194 965 individuals. The main outcome assess was the occurrence of fatal or nonfatal stroke. The summary effect associated with consumption of ≥ 3 cups of tea (green or black) per day was calculated. Regardless of their country of origin, individuals consuming ≥ 3 cups of tea per day had a 21% lower risk of stroke than those consuming less then 1 cup per day (absolute risk reduction, 0.79; CI 0.73-0.85). The results were consistent across green and black tea. The types of catechins differ between green and black tea; their total amounts are comparable because both black and green tea are derived from the same source, the catechins produced within the Camelia sinensis plant, and both have demonstrated effects on vascular function. Catechin ingestion blocked the increase in serum nitric oxide concentration in rats after reperfusion and tea had a demonstrated effect on endothelial function. Theanine is readily bioavailable from both green and black tea; crosses the blood–brain barrier and has effects on brain function; contains glutamate molecule and it might reduce glutamate-related endothelial damage. Regular tea consumption, instead of preventing evident stroke, may instead reduce the post ischemic damage to a level that results in subclinical ischemia or hidden strokes. This would result in diagnosing stroke only in individuals with more extensive post ischemic damage or a greater stroke volume.

Vitamin C lowers the risk of stroke

A 3-year intervention study [8] showed that vitamin C consumption was associated with less progression in carotid IMT in elderly men. In the study, IMT of the carotid artery and diet in elderly men were assessed. Men were randomly assigned to 1 of 4 groups: dietary intervention, omega-3 supplementation, both or neither. Results previously showed that omega-3 supplementation did not influence the IMT, thus the dietary intervention and no dietary intervention groups were pooled. The dietary intervention group had less progression in the carotid IMT compared with the controls. This group increased their daily vitamin C intake and intake of fruit, berries and vegetables. Increased intake of vitamin C and of fruit and berries was inversely associated with IMT progression.

Consumption of chocolate and risk of stroke

Consumption of chocolate has been often hypothesized to reduce the risk of CVD due to chocolate's high levels of stearic acid and antioxidant flavonoids. Reviewing studies [20] on chocolate and stroke involving 44 489 subjects who ate one serving of chocolate per week, showed that subjects who consumed chocolate were less likely to have a stroke than people who ate no chocolate; observed stroke risk reduction was 22%. People who consumed 50 g of chocolate once a week were less likely to die following a stroke than people who did not eat chocolate by 46% [6]. Debate still lingers regarding the true long term beneficial cardiovascular effects of chocolate overall. Flavonoid content of chocolate may reduce the risk of cardiovascular mortality. Review of MEDLINE publications [24] for experimental, observational, and clinical studies of relations between cocoa, cacao, chocolate, stearic acid, flavonoids (including flavonols, flavanols, catechins, epicatechins, and procynadins) and the risk of cardiovascular disease (coronary heart disease, stroke) showed that cocoa and chocolate may exert beneficial effects on cardiovascular risk via effects on lowering blood pressure, anti-inflammation, anti-platelet function, higher HDL, decreased LDL oxidation.

Physical activity in primary prevention of stroke

Mens sana in corpore sano. This famous sentence has been around for almost 2000 years. Back in the first and second century a.d., Decimus Iunius Iuvenalis, a Roman poet spoke of health, mental and physical, and their dependence on one another. But, it was not until the 1990s, when science allowed us to find proof for this idea, until the discovery of neurotrophic factors which changed around the way physical activity and brain plasticity were viewed. In 1986 Rita Levi Montalcini and Stanly Cohen received a Nobel Prize in medicine for the discovery of neurotrophins, proteins, belonging to a group of growth factors with a special effect on neurons. They signal nerve cells to grow, survive, and differentiate. One neurotrophic factor in particular, the Brain Derived Neurotrophic Factor (BDNF), important for long term memory, affects neurons in central and peripheral nervous system,

helps survival of existing neurons, growth and differentiation of new neurons and synapses. Its secretion is encouraged by physical activity.

Epidemiological and prospective studies have shown that physical activity enhances cognitive and brain function and protects against development of neurodegenerative diseases. Extensive research is going on to prove biological mechanisms that underlie such beneficial effect. Multidomain interventions could improve or maintain cognitive function in at-risk elederly people (FINGER study 2015). Prevention is the key. Greater gray matter volume, measured by MRI was found with higher aerobic activity, pointing out that it might be neuroprotective.

Scientists for centuries believed in the possibility of human brain to change. William James, in 1890, was among the first to suggest that human brain was capable for continuous functional changes, which he showed in his work Principles of Psychology [19]. It is important to keep our brain healthy as well as the body. Brain health has become a very important and recognized public health issue with a growing and aging population. Interventions are necessary from middle age further on, where we face a growing incidence of Alzheimer's disease, and other neurodegenerative disorders. Many recent studies have shown the benefits of exercise in aging populations, not only on physical health, but on brain health and functions. Exercise has become fundamental in improving and maintaining cognitive functions [4].

Physical activity is associated with lower risk of cognitive impairment, Alzheimer's disease, and dementia in general [18]. Also, a retrospective analysis showed that physical activity and behavioral stimulation reduced the risk of developing Alzheimer's disease [11]. During the 1990s, popular belief was that exercise's positive effect on the brain comes from its positive effect on overall health, especially among aged subjects. Today, we are aware of existence of neurobiological basis of these benefits, and we know that exercise has a direct effect on molecular structure of the brain. The most important and probably the most studied is the brain-derived neurotrophic factor (BDNF) which is held responsible for survival and growth of many neuronal subtypes, including glutamatergic neurons, synaptic efficacy, neuronal connectivity and use-dependant plasticity [5].

Neurotrophin-mediated response to exercise is not restricted to motor-sensory systems as expected by researchers, but showed increased levels of BDNF in the hippocampus. Hippocampus is a highly plastic structure associated with higher cognitive function, rather than motor activity. New hippocampal neurons make specific contributions to learning and memory, in part as a result of their unique neural circuitry [22]. Human studies have shown that exercise improves brain plasticity. Learning is a high-order brain plasticity activity, increases BDNF gene expression, and BDNF in turn facilitates learning [16].

Peripheral mechanisms show growing importance in activity-dependent induced changes in levels of BDNF mRNA in the brain. Components influencing this peripheral control include estrogen, corticosterone and insulin-like growth factor-1 (IGF-1).

Steroid hormones such as estrogen influence brain aging, particularly in post-menopausal women. Reduced levels of estrogen seem to compromise neuronal function, survival of neurons and decrease hippocampal availability of BDNF [28]. Just like estrogen has a positive effect on neuroplasticity, there are some factors causing negative neuroplasticity. Prolonged exposure to stress causes elevated levels of stress hormones (i.e. corticosteroids) which can be harmful to neuronal survival in hippocampus. As a response to stress (acute and chronic), neurons undergo morphological changes, dendritic atrophy and spine reduction, which have a negative impact on brain plasticity [29]. It is common belief that exercise relieves stress, reduces depression and anxiety in humans [2].

Literature shows that experience and behavior activate brain plasticity mechanisms and remodel neuronal circuitry in the brain Exercise and behavioral enrichment paradigms, such as environmental enrichment, rehabilitation training and learning, affect common endpoints in the brain, including regulation of growth factors, neurogenesis and structural changes. Similarities between these effects and exercise support the idea of existing common mechanisms regulating plasticity [19].

Exercise is simple, free, and widely practiced activity that activates molecular cascades participating in neuroplasticity. It induces BDNF encoding, neurogenesis, enhances brain vascularization, functional changes in neuronal structure and neuronal resistance to injury. Exercise increases the level of hippocampal BDNF, a brain region responsible for learning and memory. By inducing BDNF and other molecules, exercise strengthens neuronal structure, facilitates synaptic transmission, preparing activated cells for encoding.

There is a number of recent studies investigating the role of physical activity in primary and secondary stroke prevention, demonstrating its positive effect [13, 21, 17]. The research is going on and day by day there are more convincing data available on this topic.

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Mechanical Thrombectomy in Acute Stroke

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Key words:
mechanical thrombectomy, stroke, trials

Mechanical thrombectomy devices have been used for treatment of acute ischemic stroke caused by brain vessel occlusion for more than ten years. The initial results were based on case reports and case series and in the last several years on registries, mainly concerning stent retrievers. The present article presents the findings from recent international trials.

Mechanical thrombectomy (TE) devices have been used for treatment of acute ischemic stroke caused by brain vessel occlusion for more than ten years. The initial results were based on case reports and case series and in the last several years on registries, mainly concerning stent retrievers.

Randomized controlled trials (RCT) comparing iv thrombolysis (IVT) alone with TE or IVT plus TE were not available until 2013.

During the International Stroke Conference, Febrary 6–8, 2013 3 RCT's – the IMS III, MR RESCUE and SYNTHESIS trial were presented and simultaneously published in the New England Journal of Medicine (NEJM). These trials- criticized for very long recruitment periods and for using various endovascular treatment approaches did not show additional benefit of endovascular stroke therapy over IVT [1].

In the light of very positive results of registry based studies using stent retrievers, RCT's using these devices and focusing on proximal vesssel occlusions were planned and launched. In October 2014 the MR CLEAN Study from the Netherlands was presented and showed a significant benefit of TE starting within 6 hours after onset of stroke using the Soltaire device over IVT alone [2].

During the next half year a number of further studies were presented and mostly simultaneously published in the NEJM. The most important of these trials are the SWIFT PRIME study, the ESCAPE trial and the REVASCAT trial, all showing a clear and statistically significant superiority of TE-mostly plus IVT versus IVT alone [3, 4].

These results refer to the anterior circulation.

In Basilar Artery Occlusion TE is feasable and reduces mortality to around 35%, as shown in recent registry data [5].

Prospective data are however not yet available for the posterior circulation.

The ongoing BASilar artery International Cooperation Study (BASICS) trial, with currently 148 patients randomized, will hopefully answer these questions (http://www.basicstrial.com/Main.html).

The Austrian Stroke Network Thrombectomy results were published recently [5]. The TE results in Styria (Neurointervention Center Graz, catchment area 1.5 million inhabitants) are comparable to the nationwide data (Table 1).

The future development must focus on neurological and radiological facility development, ambulance logistics and also training standards for neurointerventionalists to enable health systems to provide state of the art stroke care.

A recent European consensus statement [6] of the involved medical specialties contains the relevant data and recommendations.

Up to 20% of ischemic strokes occur during sleep and present at the emergency departments in the morning hours. Since the exact duration

Table 1. Results of Mechanical Thrombectomy in Styria 2011–2014

MT Graz 2011-2/2017

Medizinische Universität Graz

Variable	Treated Patients (n=303, [illegible]) N. (%)
Recanalisation rate (TICI)	
successful recanalisation(2b-3)	256 (84,5)
Recanalisation rate (Sonography ; TIMI)*	
successful recanalisation(2-3)	208 (68,6)
Follow-up (at 3 months)^	
MRS ≤ 2	113 (43,6)
MRS 3-6	146 (56,4)

* Pill data not available in 279 cases (92,1%)

^ Pill data not available in 239 cases (80,3%)

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of symptoms is not known, thrombolysis in not possible in these cases using routine native CT imaging. Multimodal MR imaging has been used to identify wake up stroke patients in whom the 4.5 hour treatment window has not yet elapsed.

Several prospective studies are currently performed to create evidence in this field. The Department of Neurology Graz is involved in the WAKE-UP study, using MR DWI-Flair mismatch [7] and in the ECASS-4 Extend study, using MR diffusion/perfusion mismatch [8].

The ECASS-4 Extend study is ongoing with currently 119 patients randomized.

The WAKE-UP trial has stopped recruitment per June 30, 2017 with 501 patients randomized, this especially in the light oft he recently presented

DAWN study: (https://eso-stroke.org/kategorie-1/data-highlights-opening-plenary-esoc-2017).

The DAWN study sought to answer whether advanced imaging methods with MRI DWI and CT-perfusion can be used to successfully select patients for endovascular therapy, even though they present late or have an uncertain onset of symptoms. They included patients in whom brain imaging demonstrated a significant area of potentially salvageable brain tissue. Endovascular treatment significantly reduced disability compared to medically managed patients.:

There was a significant relative risk reduction (73%) in disability in 107 patients receiving mechanical thrombectomy compared to 99 with medical management (OR 2.1, 95% 1.20 – 3.12, $p<0.001$), with a number needed to treat of 2.8 to reduce disability.There was a 35% increase good functional outcome defined as mRS score of 0–2.There was no significant difference in safety outcomes between groups.

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Thrombolytic versus Standard Therapy in Acute Ischemic Stroke: A Prospective Follow up

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Key words:
ischemic stroke, intravenous thrombolysis

Cerebrovascular diseases are a global medical and social problem because of their high morbidity, mortality and disability rate. Modern treatment in the first hours of the ischemic stroke onset is directed at early recanalization of arterial thrombus, prevention of an infarct zone formation or its limitation via reestablishment of brain perfusion within the area of the so-called ischemic penumbra (a borderline zone of decreased blood flow between the viable and the necrotic tissue). Nowadays, recanalization is achieved via venous infusion of recombinant tissue plasminogen activators (rt–PAs) up to 4.5 hours after the stroke onset, as well as via endovascular treatment including intraarterial thrombolysis, thrombaspiration, etc. We present a prospective cohort study: comparative evaluation of the outcome of the acute stroke treatment in patients hospitalized at the Second Neurological Clinic of the St Marina University Hospital – Varna, between 2011 and 2016, treated with/without intravenous thrombolysis.

According to the National Centre for Health Information, in 2016 in Bulgaria there were 57 369 stroke patients; 96.6% (55 395) of them hospitalized, with prevalence of cases with ischemic stroke (AIS) – 93.5% (51 789 cases).

Thrombolysis (TL), applying rt-PA is currently an established differentiated pharmacotherapeutic treatment of AIS in its acute phase.

Undifferentiated treatment in the acute phase of ischemic stroke includes anticoagulants and antiplatelet agents. It is highlighted that this treatment can prevent the expansion of the thrombus to the ischemic penumbra; decrease the infarct size and the severity of the neurological deficit.

Based on the existing guidelines for ischemic stroke management, early application of unfractionated heparins, low molecular weight heparins or heparinoids is not recommended [19].

Heparin is recommended for the treatment of acute ischemic stroke in cases with embolism originating in the heart with a high recurrence risk, in cerebral venous thrombosis, arterial dissection of major brain arteries.

Currently in Bulgaria there is no an official national registry of acute ischemic stroke patients who underwent thrombolytic treatment. Therefore, there is no possibility to perform a national analysis of the impact of different treatments on the outcome of the disease. A significant improvement as a result of the implemented methods is reported only in publications from individual authors [8, 9]. Also, there are no correct and exact statistics about the complications arising from the implemented methods in different centers for treatment of acute ischemic stroke in Bulgaria.

Since 2011 St Marina University Hospital, has been included as a center, the first in Bulgaria, in the international register for treatment of ischemic stroke patients (SITS), and since 2016, in the ESO Registry of Stroke Care Quality (RES-Q) – Fig. 1. Because of the necessity for monitoring the safe implementation of recanalization treatment of ischemic strokes, a local register of such

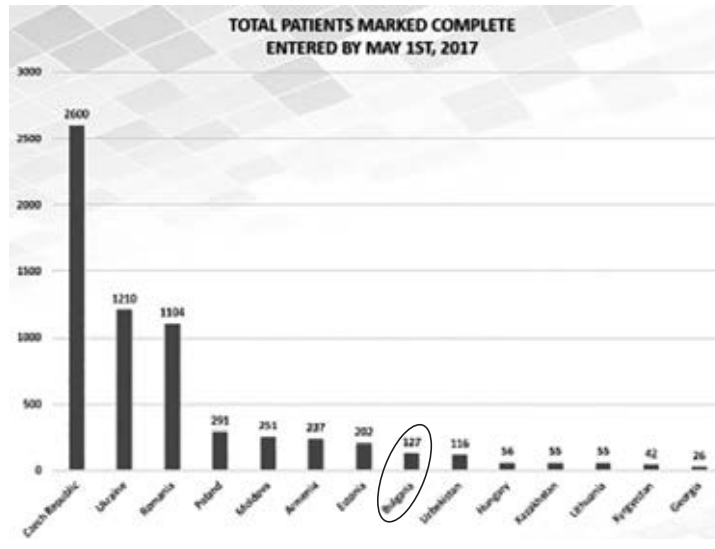


Fig. 1. *Number of patients registered in RES-Q (as reported by Robert Mikulik, 3rd Annual Meeting, ESO-EAST Program – Prague, 15 May 2017)*

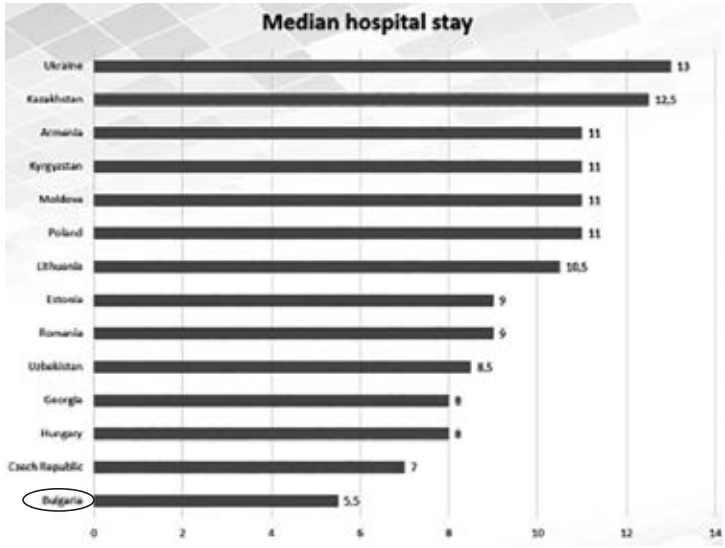


Fig. 2. *Hospital Stay for AIS patients (as reported by Robert Mikulik for the RES-Q Registry, 3rd Annual Meeting, ESO-EAST Program – Prague, 15 May 2017)*

patients has been created at the St. Marina University Hospital, Varna. The Registry is suitable for measuring continuous trends.

The possibility for comparing the results of the treatments would lead to optimization of the process at the individual centers with the aim of decreasing mortality and improving the functional outcome in AIS patients.

Since there is no a national registry of AIS patients, and for the aim of analyzing the results from our research data related to treatment optimization, we have to compare the generalized analysis of the data at the clinic to the database of the remaining centers included in the SITS international registry and the RES-Q registry.

The data from the ESO Registry on monitoring quality indicators in the treatment of ischemic stroke patients, RES-Q, confirm once again the data from the National Centre for Health Information that in Bulgaria the percentage of patients hospitalized for acute ischemic stroke is about 90%.

The in-hospital stay for treatment of stroke patients in Bulgaria is the smallest (5.5 days), as compared to the other centers in Eastern Europe, where the average number of days in an active treatment hospital is 10 (Fig. 2).

Such short hospitalization can be explained on the one hand with the standard requirements of the clinical pathway for treating ischemic stroke: minimum hospital stay – 3 days, and on the other, with the constantly increasing number of stroke patients (in 2009 – 50 678, in 2016 – 57 369, as reported by the National Centre for Health Information).

The number of acute ischemic stroke patients who during their hospitalization have been screened for existing atrial fibrillation is relatively low. About 15% of AIS patients in Bulgaria are screened, as compared to the other centers in the RES-Q Registry, where the average percentage of screened patients is between 35% and 45% (Fig. 3).

According to the SITS Registry, atrial fibrillation as a risk factor in acute ischemic stroke patients in Bulgaria is seen in about 28% of the cases. There is no significant difference in the frequency of atrial fibrillation in the other centers in the Registry (Fig. 4). As reported in scientific journals, in acute ischemic stroke patients as a result of atrial fibrillations, focal neurological symptoms are worse and lethality rate is higher [15, 20]. In order to achieve adequate treatment and secondary prophylaxis of acute ischemic stroke and atrial fibrillation patients in Bulgaria, it is necessary to increase the number of screened patients.

In Bulgaria, the percentage of recanalization procedures by intravenous thrombolysis (TL), thrombectomy, etc., remains low as compared to the centers for stroke treatment in the countries of Eastern Europe, where recanalization procedures are implemented in 20% to 30% of the hospitalized acute stroke patients (Fig. 5).

We present a comparative evaluation of the treatment outcome of acute ischemic stroke

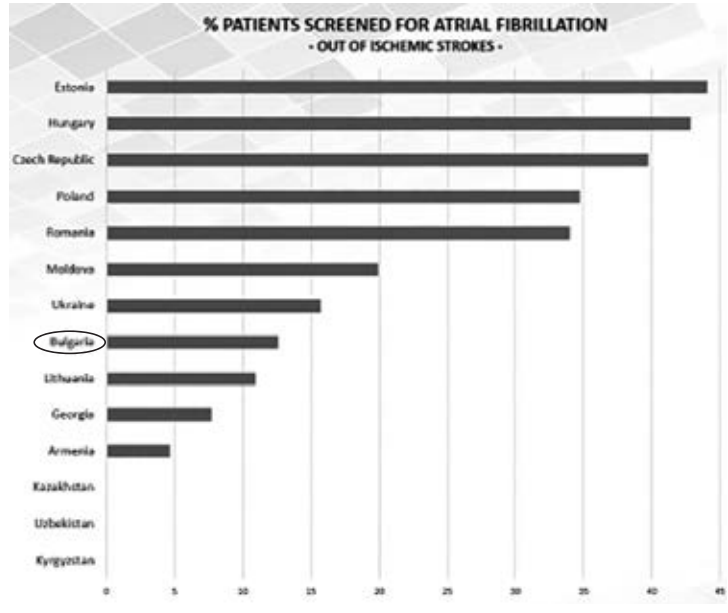
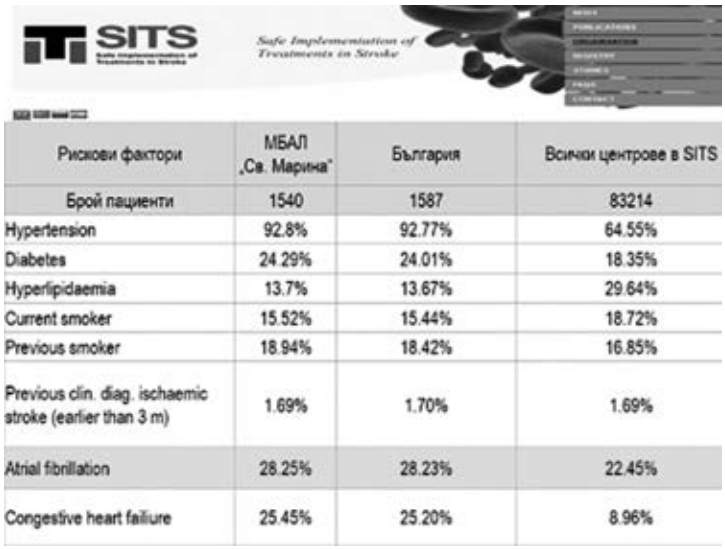


Fig. 3. *Percentage of acute ischemic stroke patients who have been screened for atrial fibrillation (as reported by Robert Mikulik for the RES-Q Registry, 3rd Annual Meeting, ESO-EAST Program – Prague, 15 May 2017)*

Table 1. Clinical characteristics of the Bulgarian cohorts

Patients	Thrombolytic treatment		No thrombolytic treatment	
	Number n (%)	Average age (years)	Number n (%)	Average age (years)
Number	384	68.79±6.7 (66.95–70.62)	1532	70.18±6.4 (69.65–70.71)
Female	173 (45%)	52.20±6.3 (44.48–59.82)	724 (47%)	48.88±6.2 (46.57–51.20)
Male	211 (55%)	47.80±6.6 (40.18–55.52)	808 (53%)	51.12±6.6 (48.80–53.43)



Рискови фактори	МБАЛ „Св. Марина"	България	Всички центрове в SITS
Брой пациенти	1540	1587	83214
Hypertension	92.8%	92.77%	64.55%
Diabetes	24.29%	24.01%	18.35%
Hyperlipidaemia	13.7%	13.67%	29.64%
Current smoker	15.52%	15.44%	18.72%
Previous smoker	18.94%	18.42%	16.85%
Previous clin. diag. ischaemic stroke (earlier than 3 m)	1.69%	1.70%	1.69%
Atrial fibrillation	28.25%	28.23%	22.45%
Congestive heart failiure	25.45%	25.20%	8.96%

Fig. 4. *Risk profile of AIS patients from the SITS Registry*

patients hospitalized at the Second Neurological Clinic at St Marina University Hospital, Varna for the period 2011–2016. The evaluation is a prospective cohort study and is

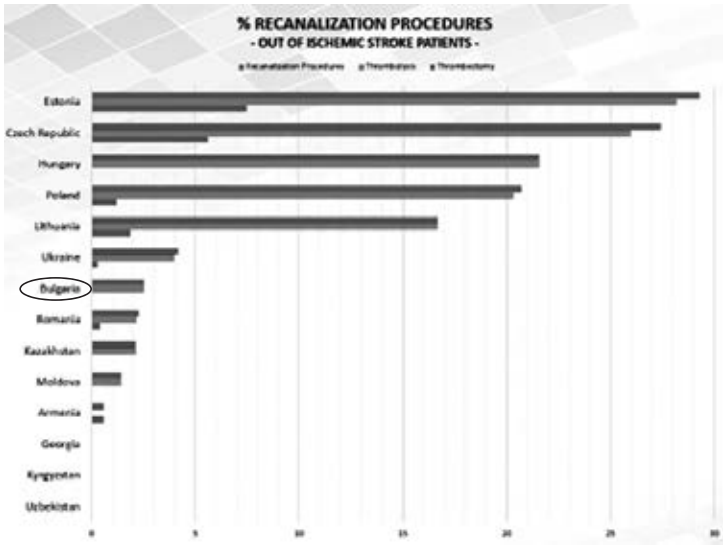


Fig. 5. *Percentage of recanalization procedures in acute ischemic stroke patients (as reported by Robert Mikulik for the RES-Q Registry, 3rd Annual Meeting, ESO-EAST Program – Prague, 15 May 2017)*

performed after a sequential introduction in our routine clinical practice of innovative treatment methods, as well as organizational restructuring for achieving optimization of the care for acute ischemic stroke patients. Two groups of patents with AIS have been studied: 384 of them (1st group) treated with thrombolysis and a control group of 1532 patients, with no thrombolytic treatment. All patients were hospitalized at the Second Clinic of Neurology with an Intensive Care Unit and Stroke unit. The clinical characteristics of the Bulgarian cohort is given respectively in Table 1.

The methods for treating acute ischemic stroke are in accordance with the effective European and national standards [4, 7, 13, 14].

The risk profile is similar in both groups (with/without TL treatment) except for hyperlipidemia and smoking, significantly higher in the TL treatment group (Fig. 6).

Table 2 shows the comparative results of the outcome after thrombolytic treatment during hospital stay or on the seventh day after the beginning of the treatment.

As a percentage ratio, the level of focal neurological deficit estimated with the NIHSS scale shows prevalence of patients with more severe motor deficit at our center as compared to the other centers in the registry.

In regard to the outcome of treatment in patients with TL during hospitalization, the data from our center, as compared to the other centers in the registry, reveal the largest percentage of patients with very good to good outcome – about 70%.

The percentage of patients with deterioration is relatively the same,

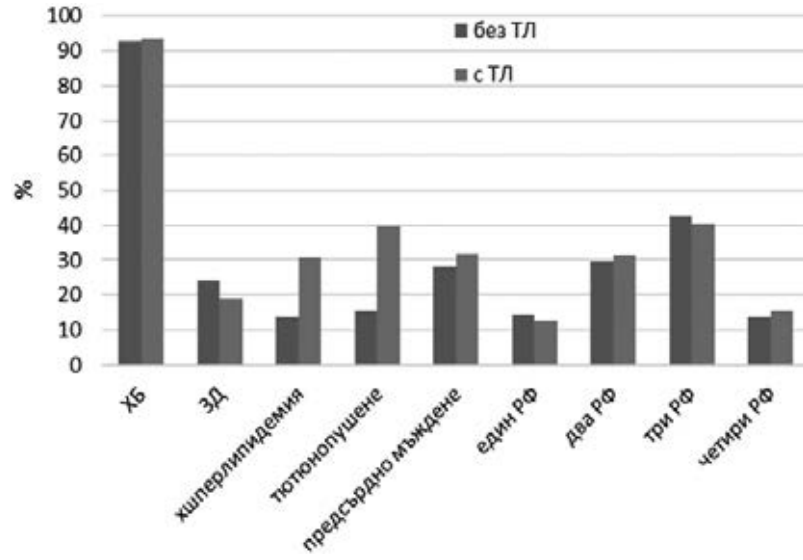


Fig. 6. *Risk profile of acute ischemic stroke patients with/without TL treatment*

about 7%, as well as the recorded deaths during hospitalization, around 6.6% (Table 2).

On admittance, focal neurological symptoms in both groups, with and without TL treatment, are relatively the same (average of 13 points on NIHSS scale). Functional independence level on discharge from hospital and on the third month after the stroke reveals significant differences in both groups. On discharging from hospital, a significant improvement in the level of neurological deficit is observed in the group with TL treatment.

The treatment outcome on the 90th day of the stroke onset reveals a slight difference in patients of both groups (with or without TL treatment), both in their functional independence, measured

Table 2. Results of the outcome of treating patients with TL during hospitalization

Clinical outcome	**Sveta Marina Varna (BGSVE) Second NC**		**Data from international centers ***	
NIHSS (24h)	Mean (CI)	Median (IQR) (N)	Mean (CI)	Median (IQR) (N)
NIHSS (24h)	11.50 (10.25–12.76)	10.00 (5.00–16.00) (137)	8.41 (8.35–8.47)	6.00 (2.00–14.00)(73503)
NIHSS (7d)	Mean (CI)	Median (IQR) (N)	Mean (CI)	Median (IQR) (N)
NIHSS (7d)	10.00 (9.55–10.45)	7.00 (3.00–13.00) (1572)	6.35 (6.29–6.40)	3.00 (1.00–10.00)(66137)
Outcome (24h)	%(CI)	n / N	% (CI)	n / N
Very much improved	25.36 (18.84–33.22)	35 / 138	30.75 (30.43–31.07)	24702 / 80339
Improved	28.99 (22.07–37.04)	40 / 138	32.08 (31.75–32.40)	25769 / 80339
No change	39.13 (31.39–47.46)	54 / 138	23.25 (22.96–23.54)	18679 / 80339
Deteriorated	1.45 (0.40–5.13)	2 / 138	8.82 (8.62–9.01)	7082 / 80339
Severely deteriorated	4.35 (2.01–9.16)	6 / 138	4.01 (3.88–4.15)	3224 / 80339
Death	0.72 (0.13–3.99)	1 / 138	1.10 (1.03–1.17)	883 / 80339
Outcome (7d)	% (CI)	n / N	% (CI)	n / N
Very much improved	37.12 (29.35–45.62)	49 / 132	41.44 (41.09–41.78)	32009 / 77249
Improved	32.58 (25.17–40.96)	43 / 132	29.40 (29.08–29.72)	22713 / 77249
No change	15.15 (10.03–22.25)	20 / 132	14.98 (14.73–15.23)	11569 / 77249
Deteriorated	3.79 (1.63–8.56)	5 / 132	4.91 (4.76–5.06)	3792 / 77249
Severely deteriorated	4.55 (2.10–9.56)	6 / 132	2.73 (2.62–2.84)	2107 / 77249
Death	6.82 (3.63–12.45)	9 / 132	6.55 (6.38–6.73)	5059 / 77249

** Data from the SITS registry*

Table 3. Patient outcome on the third month after stroke

Functional independence on the 3rd month	Sveta Marina Varna (BGSVE) Second NC		Data from international centers	
Patients with TL	**% (CI)**	**n / N**	**% (CI)**	**n / N**
mRS between 0 and 2	51.69 (42.77–60.51)	61 / 118	56.01 (55.61–56.41)	32841/ 58636
mRS between 3 and 6	48.31 (39.49–57.23)	57 / 118	43.99 (43.59–44.39)	25795 / 58636
Mortality rate on the 3rd month				
Deceased	23.73 (16.96–32.16)	28 / 118	14.59 (14.31–14.87)	8716 / 59747
Alive	76.27 (67.84–83.04)	90 / 118	85.41 (85.13–85.69)	51031 / 59747
Patients without TL therapy				
mRS between 0 and 2	36.85 (34.26–39.52)	475 / 1289	54.44 (53.04–55.84)	2652 / 4871
mRS between 3 and 6	63.15 (60.48–65.74)	814 / 1289	45.56 (44.16–46.96)	2219 / 4871
Mortality rate on the 3rd month				
Deceased	22.33 (20.14–24.68)	288 / 1290	15.83 (14.84–16.87)	785 / 4959
Alive	77.67 (75.32–79.86)	1002 / 1290	84.17 (83.13–85.16)	4174 / 4959

** Data from the SITS registry*

by the Rankin scale, and in recorded mortality in this three-month period (Table 3).

The absence of any significant difference in the disease outcome on the third month in both groups (with/without TL treatment) can be explained with the reorganization of the brain. Significant differences are observed in the mortality rate. While in dehospitalized patients who underwent TL treatment, it is about 6.6% and coincides with the data from the other centers in the registry, on the 3rd month it rises to about 24%, whereas in the remaining centers it is about 14%.

There is no exact information about the reasons leading to such significant rise in the mortality during the monitored three-month period. It may be due to belated complications from the stroke or from infections, metabolic disorders, lung thromboembolism in bedridden patients, etc., the lack of establishments for professional post-stroke recovery, where the rehabilitation started at the clinic can continue and timely measures be taken if case of changes in the basic vital signs. The absence of sufficient information and preparation of patients' relatives to take care of them can also be the reason for this rise in mortality.

Over 60% of our patients without TL treatment, on the third month have medium, moderately severe and severe disability or death (mRS 3-6), as compared to the patients in the other centers, where the prevalent percentage have no or only slight disability (mRS 0-2).

Figure 8 shows the comparative results of our research. Both in patients with or without TL treatment, on the third month after the stroke onset no significant changes in mortality rate or in disability level assessed by mRS, are observed.

The results of the research allow us to presume that mortality resulting from stroke during hospitalization in Bulgaria is not significantly higher than that in other countries.

The grounds for this are the qualification of the medical staff and the international criteria for treating strokes, adopted in Bulgaria.

The longitudinal study of patients at hospitalization, dehospitalization and on the third month establishes a significant difference in the severity of stroke, assessed by NIHSS and mRS, between the two groups (with/ without TL treatment). Thrombolysis patients are hospitalized with a severe neurological deficit (13 p. on average, measured by NIHSS scale), significantly improved in 53% of the patients at dehospitalization. This effect is also preserved on the third month of the monitoring with a tendency of another 6% of improved patients. Patients who have not undergone TL therapy are hospitalized with a more severe neurological deficit (15p. on average, measured by NIHSS scale), with recorded improvement at dehospitalization in just 38%. At the end of the third month, a significant improvement in up to 54% of the patients is established. It can be related to the processes of spontaneous recovery and brain reorganization after stroke [6].

Early mortality at dehospitalization is significantly lower in the group with TL therapy (9%), while in patients without TL it is 19%. Mortality on the third month of the disease onset is relatively the same in both groups, but the data cannot be interpreted because of absence of exact information about the reasons, which have led to the fatal outcome.

In conclusion, the complete and profound analysis of the results of the research on the AIS treatment shows that intravenous thrombolysis decreases significantly the early mortality and

severity of neurological deficit at dehospitalization, but is not associated with a significant impact on these indicators on the third month of the monitoring process, as compared to patients with undifferentiated treatment.

Our inclusion of our clinic in the international SITS and RES-Q registries has given us the opportunity to carry out comparative analysis of our results to those of the other centers in the registries.

International research has revealed that a number of objective factors limit the implementation of TL in AIS [16], among them the short therapeutic time window and numerous additional contraindications play a key role [11]. A research by Eissa et al. [17] of 2165 patients shows that because of certain contraindications, 13% of the candidates for TL have been excluded from the therapy, and according to Barber et al. [10, 12] their number is as high as 31%.

The creation of the first in Bulgaria regional register of stroke patients at St Marina University Hospital, Varna, offers the opportunity to compare the pathology and the different stages in the management of acute stroke patients with other EU countries [1, 2, 3].

The absence of a national register of acute stroke patients does not give us the opportunity to analyze on a national scale the effect of the therapy on the level of functional independence [5, 18].

The study of the disease outcome in acute ischemic stroke patients reveals that an early implementation of intravenous thrombolysis leads to a better functional outcome in the first three months after the disease onset. The comparison of the evaluated criteria on the third month of the onset supports the hypothesis for spontaneous recovery and brain reorganization.

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The Role of Arts in Enhancement of Stroke Recovery

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Key words:
arts, brain, creativity, music therapy, neuroplasticity

Stroke is a devastating illness with huge consequences to the quality of life, frequently causing motor, cognitive and mood impairment.

Due to mechanism of neuroplasticity, brain is capable of making new connections, activating new pathways and unmasking secondary roads. Music is a strong stimulus for neuroplasticity, thus having possibility to enhance recovery after stroke. fMRI studies have shown reorganization of motor and auditory cortex in professional musicians and other studies showed the changes in neurotransmitter and hormone serum levels in correlation to music. Results of numerous studies showed that listening to music can improve cognition, motor skills and moods, enhancing recovery after brain injury. In the field of visual art, brain lesion can lead to the visuospatial neglect, loss of details and significant impairment of artistic work while the lesions affecting the left hemisphere reveal new artistic dimensions, disinhibit the right hemisphere, work is more spontaneous and emotional with the gain of artistic quality. All kinds of arts (music, painting, dancing...) stimulate the brain. They should be part of the treatment processes. Work of many artists is an excellent example for the interweaving the neurology and arts.

Brain and art in health and disease

Art is a product of human creativity. It is a superior skill that can be learned by study, practice and observation. By means of art it is possible to record or describe objects, events and moments, but it is also possible to express feelings, opinions and attitudes. The Swiss painter Paul Klee said: "Art does not reproduce the visible; rather it makes the invisible, visible." Modern neuroscience has the privilege to investigate the processes of artistic performance in a healthy brain by means of modern techniques such as functional neuroimaging. Not so long ago scientists could only speculate what brain functions are involved in artistic processes by observing neurological patients. In the process of explaining the secret of creativity, a simplified theory starts with the known fact of cerebral hemisphere dominance; uncreative people have marked hemispheric dominance and creative people have less marked hemispheric dominance [16, 28]. The right hemisphere is specialized, among other functions, for metaphoric thinking, for playfulness, solution finding and synthesizing. It is the center of visualization, imagination and conceptualization, but the left hemisphere is still needed for artistic work to achieve balance by partly suppressing creative states of the right hemisphere and for the executive part of a creative process. Numerous studies investigating the brain function during the visual art activities have shown a very specific functional organization of brain areas. Different parts of visual cortex were activated, depending on the type of picture viewed (colors, objects, faces, position of objects in space, motion or static pictures) [30]. Marked hemispheric dominance and area specialization is also very prominent for music perception. Both brain hemispheres are needed for complete music experience, while frontal cortex has a significant role in rhythm and melody perception. The centers for perceiving pitch and certain aspects of melody and harmony and rhythm are identified in the right hemisphere. Left hemisphere is important for processing rapid changes in frequency and intensity of tune. Several brain imaging studies have reported activation of many other cortical areas beside auditory cortex during listening to music, which can explain the impact of listening to music on emotions, cognitive and motor processes [26, 13].

Where it comes from is crucial for some product to become a piece of art: the creativity arising from artist's brain is necessary. But it is also interesting to establish why a great number of people find a particular piece of art, music, dance or a poem beautiful. The saying "The beauty is in the eye of the beholder" is known from ancient times. Recently, T. Ishizu and S. Zeki conducted a study the results of which have revealed that a beauty experience is indeed in the beholder, though not in the eye, but in the brain [11]. As well as for the art experience, Zeki

pointed out in his book "A Vision of the Brain" that all human experience is mediated through the brain and is not solely the product of the outside world. He says "The more important the experience, the more it can reveal about the fundamental properties of the brain." [29].

Brain and music

The connection between music and brain functioning is not a modern idea. An ancient Chinese book, I Ching: "The Book of Changes/ Wisdom", that dates back to approximately 3000 years B.C. contains a saying: "Music has the power to ease the tension within the heart and to lessen and loosen obscure emotions." In the 6th century B.C. Pythagoras was analyzing pleasant tunes and found that they represented particular mathematical relations which he recognized as harmony and he supported using this harmonic music in an attempt to achieve harmony of bodily functions. His followers prescribed specific tunes and dances as a cure for mood disorders [15].

Using modern technology in science, as was already pointed out, allows an almost direct insight into the changes that music makes in human brain. Music stimulates specific regions of the brain and affects processes responsible for memory, motor control, timing and language. fMRI studies have shown reorganization of motor and auditory cortex in professional musicians. There are other studies that analyze the changes in neurotransmitter and hormone serum levels in correlation to music. Based on experience and on results of numerous studies, it is easier to understand that music is biologically and not just aesthetically, a part of human life [4, 1].

Brain plasticity was mentioned for the first time over one hundred years ago by William James and Ramon y Cajal. "Every man can, if he so desires, become a sculptor of his own brain." [12, 27]. After a long time, during the "Decade of the brain" scientists' interest in brain plasticity rose again and a lot of experiments have shown that brain is capable of making new connections, activating new pathways and unmasking secondary roads. Brain is understandably adaptable during development, but neuroplasticity shows that an adult brain is also adaptable, as a response to new and persistent stimuli or to a lesion [15, 14]. Music is one of the most frequently investigated stimuli for neuroplasticity and undeniably very strong connection between them exists. A lot of data speak in favor of the exposure of pregnant women and neonates to music promoting the development of the brain and the inner ear of child. The exposure to musical training in early life reorganizes the brain connections with consequently improved coordination and other motor skills [24]. Evidences of neuroplastic capacity of adult brain were again provided by music related studies that showed alteration of the auditory cortex after attentive listening to music for three hours a day for a longer period, superior spatial tuning in conductors and changes in motor cortical areas in adult musical learners. It was also found in injured brain [14, 7]. The most prominent connection between music and enhancement of performance or changing of neuropsychological activity was shown by studies involving Mozart's music from which the theory of The Mozart Effect was derived. The basis of The Mozart Effect lies at the superorganization of the cerebral cortex that may resonate with the superior architecture of Mozart's music [9]. Other type of music, described as "brain music" that uses frequency, amplitude and duration of musical sound similar to Chopin music is able to move the brain from an anxious to a more relaxed state and has positive effect on insomnia and fatigue (www.dhs.gov). The use of music as a cure showed its success in depressive patients after stroke. Sarkamo and colleagues conducted a study involving after stroke patients with mood disorders; one group selected for listening to self-elected music one hour daily, one listening to language on audio books and control group without listening material. After two months in the group of the music listeners a significantly lower depression rate was registered, as well as lower irritability, inertia and fewer confusion states [22]. The rehabilitation of stroke patients can be improved by incorporation of music listening in the therapy; the studies show that music stimulation increases blood flow in patients suffering from acute ischemic stroke and therefore enhances the post-stroke recovery [2]. Music is beneficial not only if listened to, but also if created, especially due to the lack of boundaries such as speech, language, psychological state or motor skills. The prospective study performed on hobby singers has shown the changes of physiologic markers of happiness during singing; the serotonin, norepinephrine and ß – endorphin levels were significantly higher after than before singing and stress hormone epinephrine was reduced by singing [5]. Neuroplasticity of the brain is crucial for rehabilitation of the patients after brain injury and it can be prompted by activity, but also by imaging of activity, due to activation of mirror neuron system. In the experiment of Pascal-Leone and co-workers one group of subjects played the piano and the other one had to just imagine that they were playing piano, with their hands being still on the table. Transmagnetic stimulation presented that the active part of the

brain was becoming larger with practice and on the fifth day in both groups the activation was similar [17]. A fMRI study showed that watching of dance movement stimulates activation of motor and other brain areas of all after-stroke patients, but in larger extent in patients with dancing experience (ballet or capoeira dancers).

There is growing evidence that artistic training improves attention and cognition. These insights arise from numerous studies with both children and adults participating and are based beyond simplified understanding that improvement can be expected just from periodical exposure to arts [23]. The key point is again activity-dependent neuroplasticity; the focused training in any of the arts, music, dance or drama activates attention networks that are a crucial part in learning and memory process. The attention networks are easier to activate with the type of arts that person is really interested in. Music has a superior effect on brain plasticity, active music training in children for a longer period of time revealed significantly better results on general measures of intelligence, in reading fluency and in performance in the geometry skills compared to results of children that didn't receive training [10, 18]. Practicing some skill increases efficiency of attention networks what besides pure cognitive improvement can enhance the executive attention skills (emotion control, empathy, impulse control...), necessary for a successful learning process.

Music can be used as a background during physical therapy in rehabilitation centers, in hospitals as well as at home. More active approach, with plying un instrument, singing (especially for patients with speech disorders such as aphasia) or more complex activity like watching a video with dancing is even more successful. Art therapy is a complex intervention capable of addressing the diverse disabilities of stroke survivors. Case studies and a few interview studies show that stroke survivors improve use of the affected limb or learn adaptational techniques through participating in art therapy. Art therapy facilitates focused attention, social interaction, communication, and emotional expression. As formal research evidence is rather limited, few explicit guidelines emerge for achieving best practice with stroke survivors. Mixed-method research might provide the foundation for art therapy to become a better recognized component within stroke rehabilitation programs [20].

Brain and visual arts

When a person suffers a stroke, the symptoms depend on the site of injury. If there is a right hemisphere lesion, impairment of spatial tasks, left-sided visuospatial neglect, impaired facial recognition and spatial organization and perspective impairment are present. In painting style compensatory changes develop with the creation of the wider scenery of landscapes and larger figural compositions [3]. The German painter Anton Räderscheidt suffered the right hemisphere stroke after which a substantial change in his painting style was evident; noticeable was left sided hemianopia and neglect, and previously very realistically painted figures and persons after stroke were usually deformed, intense and in bright colors (www.raederscheidt.com). Federico Fellini, an Italian film director, painter and cartoonist suffered a stroke at the age of 73 in the right middle cerebral artery territory with the severe left – sided motor and sensory deficits, left inferior quadrantopia, but without anosognosia, prosopagnosia or cognitive deficits. These deficits manifested on his sketches after stroke with the neglect of the left side of drawing area, but after two months the good recovery or compensation of vision was apparent in new drawings with equal amount of details on both sides of the area [6, 8].

In a left hemisphere stroke patient aphasia, right-sided hemiparesis and loss of executive functions are present. After starting to use nondominant hand, artistic work of many artists becomes disinhibited, more impressionist or more intense and expressive. Katherine Sherwood, an American painter suffered a severe dominant hemisphere stroke at the age of 44. From then she paints with her left hand and these new paintings differ significantly from pre-stroke work, she herself claims that her early work was constricted, tripped up by conscious intent and recent work unburdened, flows freely from her subconscious, uninhibited by consciousness. She even achieved rather more acclaim and financial success after the stroke [25, 19]. After a left hemisphere stroke the Swedish painter and sculptor Carl Fredrik Reutersward also experienced a more disinhibited work, manifested by using of brighter colors and "softer" shapes. So, the effect of stroke on artistic performance depends on the site of the lesion; the right hemisphere lesion leads to the left sided visuospatial neglect, loss of details and significant impairment of artistic work while the left hemisphere lesions reveal new artistic dimensions, disinhibit the right hemisphere, work is more spontaneous and emotional with the gain of artistic quality.

Sometimes brain and neurological illnesses themselves can be an inspiration for artwork. In his book "Brainy Drawings" the Croatian artist Ivan Šarić raises awareness of the brain complexity, neurological conditions and importance of prevention and the right treatment of brain

disorders through numerous witty yet engaged sketches of the brain.

Conclusion

In the field of visual art it is obvious and encouraging that a disease is not an inevitably debilitating condition. On one side, an illness can seriously restrain living activities, but on the other, the creative side gives new opportunities for something that the conscious mind is not aware of.

The connection between brain and music is strong and bidirectional. As Oliver Sacks, professor of neurology and a writer who extensively studied the effect of music on human health wrote: "We turn to the music, we need it, because of its ability to move us, to induce feelings and moods, states of mind." [21].

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Treatment of Intracerebral Hemorrhage – a Practical Approach

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Key words:
diagnosis, Neurophysiology, peripheral nervous system, rehabilitation, ultrasound

Intracerebral hemorrhage is the most devastating subtype of stroke. It affects approximately 2 million patients worldwide every year and is a major cause of morbidity and mortality. After decades of research there is still no specific evidence based treatment strategy for this disease. However, research has contributed to a better understanding of the pathophysiology of intracerebral hemorrhage, and has facilitated the development of different treatment approaches addressing different pathophysiological mechanisms. The present article reviews some of the latest research investigating treatment strategies for ICH and IVH and comments on the practical relevance of those data, including topics as blood pressure management, hemostasis, surgery, hypothermia, intraventricular fibrinolysis and lumbar drainage.

Introduction

Spontaneous intracerebral hemorrhage (ICH) accounts for 10-15% of all strokes [47, 30]. With an annual incidence of 10-30 per 100 000 population ICH affects approximately 2 million patients worldwide every year [45]. While incidence of ICH is comparable between white, black and Hispanic people, it is about two times higher in eastern and south-eastern Asians [61]. Older people are at higher risk to suffer ICH. With every additional age decade, incidence of ICH increases almost twice. It comprises only 1.9 per 100 000 person-years for people younger than 45, 36.5 for 55-64 year-olds and 196 per 100 000 person-years for people older than 85 [61]. Considering the trends of current demographic development and the increasingly ageing population in the western world, ICH is expected to gain further importance as a public health problem in the future [33].

Up to 70-90% of ICH are caused by rupture of small vessels chronically damaged by hypertension. Typically, such primary hypertensive ICH are located in the basal ganglia (28-42%) and the thalamus (10-26%) [6, 57]. Lobar ICH, as well as cerebellar and brainstem ICH are less frequent [57]. Secondary ICH are associated with vascular malformations, aneurysms, tumors, secondary hemorrhagic transformation of ischemic areas, amyloid angiopathy (especially in older patients), drug abuse, or disturbances of coagulation, including patients treated with oral anticoagulants (up to 20% of all ICH) [13, 57]. According to their variable etiology, such bleedings are often atypically located.

Prognosis of ICH is worse as compared to ischemic stroke, including a higher mortality reaching approximately 40% within the first 30 days after the bleeding, and a higher morbidity [61]. Only approximately 20% of ICH patients are functionally independent at 6 months [49]. A recent analysis of the Global Burden of Disease Study focusing on the neurological field confirmed the important role of so called "hemorrhagic strokes" (a term including ICH and SAH) as the cause of the highest mortality and morbidity as compared to all other diseases from the neurological spectrum [8]. Looking at Disability-Adjusted Life-Years (DALY), hemorrhagic strokes are the number one DALY cause (35.7% of DALY caused by any neurological diseases), followed by ischemic stroke with 22.4%, migraine (12.7%), epilepsy (9.9%), dementia (6.4%). Diseases like Parkinson's disease (1.1%) or multiple sclerosis (0.6%) cause a comparatively low burden of DALY. For better understanding a DALY can be described as the loss of one healthy year of one's life.

Clinical studies have identified multiple factors associated with higher mortality and worse outcome in ICH. Older age and lower Glasgow coma scale (GCS) score at presentation have been almost uniformly reported as independent negative prognostic predictors [5, 9, 32, 58]. Other important factors independently associated with unfavorable outcome are ICH volume [5], hematoma growth [10], intraventricular hemorrhage (IVH) [4, 55, 59], hydrocephalus [4, 11], and perihemorrhagic edema [53]. While age and GCS represent more or less all-encompassing surrogate parameters accounting for comorbidity and stroke severity in general, the identification of specific ICH related prognostic predictors has contributed to a better understanding of the role

and importance of different pathophysiological mechanisms in ICH and has led to the development of specific treatment strategies. Despite of this increasing knowledge, research has not yet brought up a specific treatment for ICH patients proven in a large phase III clinical trial and suitable for recommendation for the clinical routine. Most of the current recommendations and guidelines (e.g. AHA/ASA, ESO) [21, 54] are based on lower-level evidence or expert opinions. The present review will focus on some treatment strategies including blood pressure management, hemostasis management and treatment of OAC-associated hemorrhages, surgery, treatment of brain edema, and fibrinolysis for IVH and lumbar drainage for communicating hydrocephalus after intraventricular hemorrhage (IVH).

Blood pressure management

It is well documented in literature that hypertensive blood pressure levels in the early phase of ICH are associated with more ICH growth and worse clinical outcomes. Based on this background, blood pressure control appears to be an attractive therapeutic option that does not require special expertise and is therefore widely available. Guidelines on the management of blood pressure in ICH patients have been very conservative in their target recommendations, which until very few years ago ranged about systolic values of 160-180 mmHg. Very aggressive blood pressure management in ICH may indeed be a double-edged sword, because those patients usually have a vascular risk profile and consecutively increased risk for ischemic strokes. Meanwhile, however, it is well established that autoregulation is preserved in the perihemorrhagic tissue, although blood flow in those areas is reduced, and lower blood pressure levels can be tolerated without danger of ischemia in the perihemorrhagic zone.

The phase II INTERACT trial that has been published several years ago (Anderson et al., 2008) could demonstrate in totally 404 ICH patients that blood pressure reduction to target levels of 140mmHg is safe. There was even a trend towards less hemorrhage growth in the treatment arm. Expected with interest, the phase III INTERACT 2 trial was recently published [3]. This was a multicenter, randomized, controlled trial in 2839 patients with spontaneous ICH and high blood pressure (150 mmHg systolic BP) within 6 hours after symptom onset. The study compared two different blood pressure management regimens. In the intensive blood pressure reduction group the target systolic blood pressure was <140 mmHg within 1 hour after randomization. The control group was treated according to the guideline recommendations at the time when the study was conducted (target systolic blood pressure <180 mmHg). The primary endpoint of the trial compared the proportion of patients that were dead or severely disabled (mRS 3-6) 90 days after the bleeding event. This was the case in 52% of the patients treated with intensive blood pressure lowering, as compared to 55.6% in the control group (p=0.06). Although this is a strong trend in favor of the intensive regimen, this result was not statistically significant. Another predefined analysis, the ordinal analysis of the distribution of scores on the mRS scale, showed a marginally significant benefit of intensive blood pressure lowering. Contrary to the results of the phase II study, INTERACT 2 did not demonstrate statistically significant differences in hemorrhage growth between the two groups. A very important aspect of this trial was the repeated demonstration of safety of the intensive blood pressure management regimen. None of the safety endpoints showed statistically significant differences between the two groups, especially considering ischemic strokes. In summary, INTERACT 2 showed that intensive blood pressure lowering to target systolic levels of 140mmHg does not increase adverse events and shows a strong trend towards improvement of clinical outcome in patients with spontaneous ICH. Meanwhile, many sub-analyses of INTERACT 2 have been published. One of them addresses the influence of blood pressure variability on clinical outcome. The study demonstrated that high blood pressure peaks, as well as higher blood pressure variability was associated with worse outcome. This could mean that the positive effect of blood pressure lowering may be further enhanced with a strict blood pressure control and avoidance of high variability in the acute phase [36]. The results of INTERACT 2 led to changes in the ESO and AHA/ASA recommendations for systolic blood pressure management of ICH to <140 mmHg [21, 54]. A shortly published retrospective analysis from Germany that deals with oral anticoagulant associated hemorrhage also showed a possible negative effect of high blood pressure values on mortality and outcome within the first hours after ICH [29]. Therefore, the recommendations for intensive blood pressure management seem justified for this group of patients while there is no better quality data. INTERACT was performed by an Australian team and recruited patients mainly in China. Therefore, the US American ATACH II trial [46], which was performed in the USA and included 1,000 patients, was eagerly expected in order to achieve certainty about the generalizability of the INTERACT results. ATACH II used a very similar protocol in terms

of target blood pressure values, however, while INTERACT used a pragmatic approach allowing different antihypertensives, ATACH allowed only i.v. nicardipine. Another important difference between INTERACT and ATACH is that in ATACH II, although the blood pressure targets were defined similarly as in INTERACT, the actual achieved levels in the control group were similar to the intensive management arm in INTERACT, whereas the intensive arm in ATACH was at mean levels of 120 mmHg systolic blood pressure. This comparison between "intensive" (as achieved in INTERACT) and "very intensive" blood pressure lowering did not result in a statistically significant difference in clinical outcome, even a trend was not observed. There were, however, significantly more severe adverse events in the treatment arm. After ATACH II was published in 2016, most experts did not see a necessity to change the current recommendations for the clinical routine again based on this trial. ATACH, however, opened more space for discussion on blood pressure lowering in ICH, especially with respect to possible harms beyond a "sweet spot" of a safe target value. Those discussions are reinforced by recent findings of MRI in patients with ICH. A retrospective study by Prabhakaran and colleagues [44] described distant small ischemic lesions (areas of restricted diffusion on DWI imaging) and found a correlation between those lesions, extensive blood pressure reduction, and worse clinical outcome. Those findings were recently confirmed in a larger prospective cohort from the ERICH study [25], demonstrating that roughly a quarter of all spontaneous ICH patients show such lesions on MRI. Summarizing those trials, 140 mmHg seems to remain a safe target for blood pressure management in acute ICH and avoiding strong variability of blood pressure seems also to be very important in such patients. Future studies should include MRI imaging in order to estimate the role of DWI lesions and their association with blood pressure lowering.

Hemostasis

The rationale of hemostasis in the acute phase of ICH lies in the optimization of clotting and a possible avoidance of early hematoma growth. Recombinant activated factor VII (rfVIIa) was originally developed for treatment of hemophilia related bleeding conditions [20]. RfVIIa promotes hemostasis at sites of vascular disruption thereby limiting hematoma growth after ICH. This effect has been demonstrated in a randomized placebo controlled phase 2b clinical study [37]. Doses of 80 and 160 µg/kg administered within 4 hours of the initial bleeding event could significantly reduce hematoma growth, as compared to placebo. This was the primary outcome measure chosen for that trial. The study was even able to show a significant benefit in terms of mortality and functional outcome associated with use of rfVIIa, despite a 5% increase in arterial thromboembolic events [37]. Therefore, the result of the phase III clinical trial (FAST) was disappointing, for it could not find a significant difference in the primary outcome measure death or severe disability, despite of confirming the effect of hemorrhage growth reduction and the safety profile of rfVIIa considering thromboembolic events [38]. A second look at the data from the FAST trial however raises hope that a selected subset of patients may anyway benefit from rfVIIa treatment. A post-hoc analysis, from which patients known to be at high risk for poor outcome at baseline were excluded (ICH >60 ml, IVH >5 ml, age >70 years, treatment later than 2.5 hours), could show a strong trend towards improved outcome and a twofold reduction in hematoma growth in the selected collective treated with rfVIIa [39]. On that basis the routine use of rfVIIa for treatment of ICH cannot be recommended. Currently, several ongoing clinical trials investigate the use of hemostasis in spontaneous ICH using other agents, e.g. tranexamic acid.

While not indicated for spontaneous ICH, hemostasis with fresh frozen plasma (FFP) or prothrombin complex concentrate (PCC) is the first line treatment strongly recommended for oral anticoagulant associated ICH [21]. A small European randomized controlled trial (INCH trial) [56] published after the above-mentioned guideline, showed a clear advantage of PCC over FFP in patients with vitamin K antagonist associated ICH. A recent large retrospective analysis from Germany (RETRACE) has shown that fast treatment of such patients with INR normalization <1.3 together with a well-controlled blood pressure is essential for reduction of hematoma growth and prognosis [29]. As far as data are available for ICH associated with the new class of direct oral anticoagulants (NOAC), those bleedings seem to have a quite similar course and prognosis as vitamin K antagonist associated ICH. Therefore, experts concordantly recommend antagonization with either specific antagonists as idarucizumab for dabigatran, or PCC for the other NOACs [14, 43].

Surgery

From the pathophysiological point of view, early surgical removal of intracerebral hemorrhage seems justified for several reasons. On one hand, it could reduce the space occupying effect

of the hematoma and relieve the pressure on surrounding brain tissue. On the other hand it could prevent extensive release of blood breakdown products into the surroundings of the hematoma thereby preventing secondary damage to initially non-affected tissue.

The largest recent randomized controlled trial comparing early surgery versus initial conservative treatment in ICH (Surgical Trial in IntraCerebral Hemorrhage – STICH) included over 1000 patients and failed to demonstrate any benefit from the early surgical approach [40]. Considering the strong pathophysiological background of clot removal this result was rather disappointing. Although the STICH trial provides the best data available on surgical treatment of ICH up to date, some major methodological issues have been subject of criticism: the so called "uncertainty principle" of patient enrolment, according to which patients were considered for randomization only if the treating neurosurgeon was uncertain about the benefit of surgical treatment – a question, the study actually intended to answer. Furthermore, the study protocol allowed patients allocated to the "Initially Conservative Treatment" arm to receive delayed surgery after suffering secondary deterioration. This was the case in one fourth of those patients. Nevertheless, subgroup analyses have shown that patients with lobar hematomas located near (≤ 1 cm) the cortical surface tend to benefit from early surgery. On that basis the STICH II trial was conducted in order to compare surgical with initial medical treatment in this subgroup of patients. Unfortunately, some major methodological issues as the "uncertainty principle", were kept in this trial, which was recently published [41]. STICH II included patients with superficially located lobar ICH with a volume between 10-100 ml and symptom onset within 48 hours before randomization. Patients with IVH were excluded. Early hematoma removal within 12 hours after randomization was compared with initially conservative management. The primary endpoint of this trial was the clinical outcome (Glasgow Outcome Scale Extended – GOSE) 6 months after the event, evaluated by using a prognosis-based method in order to consider important strong prognostic predictors as age, GCS and initial ICH volume. Mortality was analyzed as a secondary endpoint. Of totally 601 included patients, 307 were randomized into the early surgery group. As in STICH, the percent of patients from the control group that were later subjected to surgery, most often due to secondary deterioration, was relatively high (62 of 294, 21%). Craniotomy was the most frequently used surgical method (in 98% of patients). STICH II also did not bring up a significant result. The primary endpoint did not differ between the two groups (p=0.37), in terms of mortality there was a non-significant trend in favor of the early surgery (5.6% absolute risk reduction, p=0.095). A subgroup analysis was not conclusive. Only patients with a worse prognostic estimation based on the criteria defined by the authors seemed to benefit from surgical treatment. As the study was planned to detect a difference of 12%, the statistical power was not sufficient in order to show a significant result at the level of the detected trends. Mendelow & al. presented within the publication of STICH II an updated meta-analysis of randomized controlled trials on surgery in ICH. In this meta-analysis the authors included totally 15 studies of different size and quality published between 1961 and 2013. Most of the patients for this meta-analysis were contributed by both STICH trials. In summary, a significant benefit was found in favor of surgical treatment with an OR of 0.74 (95% CI 0.64-0.86, p<0.0001) for bad outcome, however heterogeneity was also significant for the included trials. The sub-analysis of individual data for patients with lobar hemorrhage without IVH showed a trend towards benefit from surgery, however it was not statistically significant (OR 0.78; 95% CI 0.59-1.02, p=0.07). In summary, we can conclude that the results of STICH and STICH II were disappointing and it cannot be excluded that a potential treatment option for ICH possibly could not be sufficiently investigated due to weaknesses in trial design. Although the meta-analysis by Mendelow et al. shows beneficial trends for surgery, the quality of the presented data does not allow a straightforward recommendation for the clinical routine. Therefore, surgery still remains an option for ICH patients, based only on an individual decision.

Open craniotomy may be associated with damage due to the large access to the hematoma and thereby cause additional harm, which may weigh out the benefit of hematoma removal. Considering this background, minimally invasive surgical techniques (MIS) for ICH appear an attractive alternative. In recent years several, mostly small clinical trials investigating stereotactic or endoscopic MIS have been published [7, 15, 19, 28, 31, 63]. Those data are mostly very optimistic, but only provide the basis for further research and do not justify practical recommendations. Another interesting approach is the combination of minimally invasive insertion of a parenchymal catheter into the intracerebral clot with following thrombolysis with small doses of rtPA and hematoma drainage [16]. This treatment is being investigated in the MISTIE study program. The phase II study from this

program was recently published [18] and showed optimistic results considering safety issues. There was also a trend towards improvement of clinical outcome. The phase III MISTIE trial started in December 2014 and has already recruited a very large proportion of the planned sample size of 500 patients. The results of this trial are eagerly expected and will probably be made available in 2018.

Edema treatment

Osmotherapy

The use of osmotic agents for treatment of cerebral edema is based on the assumption that osmotically active substances could facilitate the transfer of water from the interstitium into the bloodstream thereby reducing the space-occupying effect of perihemorrhagic edema. Osmotic agents routinely used in neurocritical care include mannitol, glycerol, and hypertonic saline. To date there are no high quality data in support of those treatment options in patients with ICH. A smaller clinical study showed that continuous hypertonic saline may reduce edema and improve outcome in patients with ICH treated in neurological ICU [62]. A post-hoc analysis of the INTERACT 2 trial showed no convincing effects of mannitol on the clinical course after ICH [64].

Hypothermia

Hypothermia has been subject of research in experimental ICH models in the recent past and several rodent studies have reported reduction in inflammation, oxidative damage, blood brain barrier disruption and perihemorrhagic edema using prolonged therapeutic hypothermia [12, 24, 35]. The clinical application of mild therapeutic hypothermia (35°C for up to 10 days) in patients with large ICH has been investigated by one research group from Erlangen, Germany [27, 52]. The authors of those studies describe a marked reduction of perihemorrhagic edema evolution and a lower mortality in treated patients as compared to historical controls. Hypothermia in ICH is currently being further investigated in ongoing trials [26].

Specific treatment of intraventricular hemorrhage

Intraventricular fibrinolysis

Additional IVH is a frequent complication of ICH affecting up to 50% of ICH patients. The presence of IVH alone is a strong negative prognostic predictor. If, however, the third and/or fourth ventricles are affected by the ventricular clot, IVH can cause the life-threatening complication of acute obstructive hydrocephalus. In this case, the placement of an external ventricular drain (EVD) is necessary. EVD alone is often not sufficient, because especially in more severely affected patients the catheter is frequently obstructed by blood clots [1]. Although it seems paradoxical at first glance to treat a hemorrhage with fibrinolytics, the concept of intraventricular fibrinolysis (IVF) has been tested in the experimental setting since the 1980s and first successful treatments in clinical cases have been reported in the early 1990s [48]. The rationale of this treatment consists in the degradation of the ventricular clot by injection of low dosed fibrinolytic substances (e.g. rtPA or urokinase) into the EVD at a time point, where the bleeding has already stopped and the clot is consolidated. This way the functionality of the drain can be kept and the degradation and drainage of the intraventricular clot can be fastened. Low quality data from small, mostly nonrandomized clinical trials on IVF in patients with IVH that have accumulated over the past few decades show trends of reduction of mortality and improvement of clinical outcome, as compared to EVD alone or conservative treatment (no EVD) [48]. A large phase III randomized, blinded, placebo-controlled clinical trial (CLEAR III) investigated the efficacy of IVF in 500 patients with IVH and acute obstructive hydrocephalus [17]. The study finished recruiting patients in 2014 and was recently published. The primary outcome of the trial, namely the difference in the proportion of patients with good functional outcome (mRS 0-3) 180 days after the event, showed no statistically significant difference between intraventricular rtPA and placebo. There was, however, a significant reduction in mortality (absolute risk reduction of 10%, $p=0.006$) in favor of the rtPA group. In a subgroup analysis patients with more severe IVH (>20 ml) from which >80% was removed, significantly benefited from IVF with rtPA. Although the primary endpoint of CLEAR III was not conclusive and IVF cannot be generally recommended for patients with IVH and obstructive hydrocephalus based on that trial, the reduction in mortality and the possible benefit of severely affected patients could support individual treatment decisions in the clinical routine.

Lumbar drainage

A large proportion of patients develop communicating hydrocephalus after IVH, and up to 30-60% of them require shunt surgery, because of unsuccessful weaning off the EVD [22, 60]. Even in the setting of IVF there is frequently a prolonged need for external CSF drainage, after obstructive hydrocephalus has been treated and communication between the ventricles and the

subarachnoid space has been restored [50]. Longer EVD duration is however associated with an exponentially increasing risk of ventriculitis [34]. Therefore, in patients with communicating hydrocephalus after IVH, lumbar drainage (LD) may represent a less invasive and simple alternative for extracorporeal CSF drainage with a lower complication profile, as compared to EVD [22, 23, 50]. The capability of LD to replace EVD in communicating posthemorrhagic hydrocephalus has been demonstrated in several small studies [22, 23, 50]. The success of the procedure has led to a substantial reduction of the EVD exchange rate in those patients. Lumbar drainage, especially applied early after IVF, may also reduce the incidence of permanent hydrocephalus and ventriculo-peritoneal shunts in patients with ICH and severe IVH, as shown in a prospective case series and confirmed in a randomized controlled trial [50, 51]. This effect is possibly explained by the rapid clot resolution using IVF, but also by early washout of blood and blood breakdown products from the site of CSF resorption via LD, namely the subarachnoid space. Considering the high malfunction, complication and revision rates of ventriculo-peritoneal shunts [42], prevention of their usage is certainly a benefit for those patients. The available data are however not sufficient to estimate the possible impact of the combination of IVF and early LD on functional outcome.

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Brain Parenchyma Neurosonology

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Key words:
basal ganglia,
deep brain stimulation,
substantia nigra,
transcranial ultrasound

Transcranial B-mode sonography (TCS) is a non-invasive, low-cost, short-duration neuroimaging method that allows high-resolution imaging of deep brain structures in patients with movement disorders. With contemporary high-end ultrasound systems, image resolution of echogenic deep brain structures can even be higher on TCS than on magnetic resonance imaging (MRI). Hyperechogenicity of the substantia nigra (SN), a TCS finding seen in about 90% of patients with idiopathic Parkinson's disease (PD), is already present in presymptomatic disease stages and indicates an increased risk of developing PD, especially if present in combination with other risk markers. The TCS finding of SN hyperechogenicity well discriminates PD from other Parkinsonian disorders such as multiple-system atrophy and welding-related Parkinsonism. In turn, normal SN echogenicity in combination with lenticular nucleus hyperechogenicity indicates an atypical Parkinsonian syndrome rather than PD with a specificity of more than 95%. TCS detects characteristic basal ganglia changes also in other movement disorders such as lenticular nucleus hyperechogenicity in idiopathic dystonia and Wilson's disease and caudate nucleus hyperechogenicity in Huntington's disease. Reduced echogenicity of midbrain raphe is frequent in depressive disorders and correlated with both suicidal ideation and responsiveness to serotonin reuptake inhibitors. TCS reliably and safely displays deep brain stimulation electrodes in patients with movement disorders and allows intra- and postoperative monitoring of electrode location. Upcoming technologies such as digitized image analysis and TCS-MRI fusion imaging will promote novel diagnostic applications of TCS in neurodegenerative brain disorders.

Clinical applications

Transcranial B-mode sonography (TCS) of the brain parenchyma is a non-invasive neuroimaging method that allows high-resolution imaging of deep brain structures in patients with degenerative brain diseases [8]. Beside transtemporal axial and coronal imaging planes also transfrontal sagittal planes can be applied for special diagnostic purposes [9]. Hyperechogenicity of substantia nigra (SN), found in about 90% of patients with idiopathic Parkinson's disease (PD), is already present in presymptomatic disease stages. The results of longitudinal studies suggest that TCS of SN may serve as a screening tool for detecting subjects at risk of developing PD [2, 3]. Studies of our and other groups show that the combination of TCS with simple olfaction and motor tests already at very early disease stages discriminates PD from other Parkinsonian disorders. In turn, normal SN echogenicity in combination with lenticular nucleus hyperechogenicity indicates an atypical Parkinsonian syndrome rather than PD with a specificity of more than 95% [2, 10]. SN hyperechogenicity has also been reported in spinocerebellar atrophy type 2 with Parkinsonism and the parkinsonism-dominant variant of X-linked dystonia-parkinsonism [6, 11]. TCS detects characteristic basal ganglia changes also in other movement disorders such as lenticular nucleus hyperechogenicity in idiopathic dystonia and caudate nucleus hyperechogenicity in Huntington's disease [12]. Lenticular nucleus hyperechogenicity in Wilson's disease has been proven histochemically to be caused by copper accumulation, while the same TCS finding is caused by iron accumulation in hereditary disorders with brain iron accumulation such as PKAN and MPAN [13]. Reduced echogenicity of midbrain raphe is frequent in depressive disorders and in migraineurs [1, 5]. An elegant application of TCS is the intra- and postoperative localization of deep brain stimulation electrodes in patients with movement disorders [14, 15].

Method

For TCS of brain parenchyma an optimized ultrasound system equipped with a 2.0- to 3.5-MHz phased-array transducer is used. The system settings should be checked, especially the dynamic range should be set at 45-50 dB. One should keep in mind that with the ultrasound transducers applied for TCS the highest image resolution is achieved in an image depth of 5-9 cm (focal zone of transducer) [8]. Due to the physical characteristics of ultrasound beam the image resolution in axial direction (i.e. along the axis

of ultrasound propagation) is about 2- to 3-fold higher than in lateral direction (usually about 0.7×2 mm), which is the cause also of some typical imaging artifacts (e.g. the enlargement of small, highly echogenic structures in lateral direction). Distinct measurements such as the assessment of echogenic areas of small brain structures are influenced by image post-processing technologies and can therefore differ between different ultrasound systems. That is why normal ranges especially for echogenic area of the SN need to be obtained for each different ultrasound system.

For TCS investigation the patient is placed in supine position on an examination chair layer, which should be equipped with a variably adjustable, lean part. For the usually performed transtemporal investigation the TCS transducer is placed on the right temple near the ear and parallel to the orbitomeatal line in order to obtain a standardized axial view of intracranial structures. It is important to identify and keep the optimum bone window for insonation. For this, the transducer is moved near the anterior helix of the ear conch, searching for the position with best available visualization of brain structures and contralateral skull bone. Once the optimum position has been found it is kept by pressing the transducer but also the small finger/ulnar edge of the hand firmly at the patients' head throughout the whole examination. Even if applying optimum system settings (ultrasound frequency, dynamic range, image brightness, time gain compensation) assessment of intracranial structures may be not or only partially possible due to insufficient transtemporal bone window which is found in 5-40 % of patients depending on age, sex and geographic origin [2, 12].

In neurodegenerative diseases transtemporal TCS is usually carried out in standardized axial imaging planes. For some diagnostic questions TCS is additionally performed in semi-coronal and coronal or transfrontal axial und sagittal imaging planes [9], e.g. for the assessment of corpus callosum or the localization of deep brain stimulation (DBS) electrodes [14, 15]. TCS findings can be categorized into two types. The first is the semi-quantitative or quantitative assessment of ***echogenicity*** of brainstem structures (SN, red nucleus, midbrain raphe) and basal ganglia (thalamus, lenticular nucleus, head of caudate nucleus), optionally also of cerebellum and other deep brain structures (e.g. white matter, corpus callosum, hippocampal region). The second is the measurement of widths (optionally also the cross-sectional area) of 4th ventricle, 3rd ventricle, frontal horns of lateral ventricles and if needed the cella media. Upcoming technologies such as digitized image analysis and TCS-MRI fusion imaging promote novel diagnostic applications of TCS [7, 14].

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Ultrasound of Peripheral Nerves

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Electrodiagnosis is the main tool in assessing nerve function and hence is crucial in the diagnosis of nerve involvement. In the last years, an improved resolution, increased portability and a wider access to ultrasound (US) have made this tool useful in assessing peripheral nerve impairments as entrapments, tumors, extrinsic compressions, traumatic lesions, immune-mediated and inherited neuropathies.

A wide literature shows that US integrates neurophysiological assessment in routine practice: by a combined use of electrodiagnosis and US we obtain more information than we do if they are separately used. If neurophysiology allows detecting nerve function, US provides detailed imaging of nerve morphology and size and of the surrounding structures. A multidimensional evaluation of peripheral nervous system impairments improves diagnostic precision and therapeutic accuracy, even providing data about prognosis and disease evolution.

The main quantitative measure that US provides, owing to its sensitivity, is the nerve cross-sectional area (CSA), which is the area of the nerve structure visualized by a transverse US scan, calculated using the ellipse or the tracing method. Usually, an increased CSA indicates nerve involvement. Besides this, we can evaluate echogenicity, alteration of nerve elements (e.g. fascicles), and variations in nerve shape. US report is based on characterization of nerve abnormalities and localization and extension of these findings.

Introduction

Ultrasound (US) systems known as SONAR were used in submarines for object detection [5]; after the World War, the same technology was used in medical practice as a treatment tool, based on heat production by US with beneficial effects upon tissues [6].

During the last years, in scientific literature, peripheral nerve and muscle imaging has become a topic of high interest especially for diagnosis of peripheral nerve diseases: neurophysiology keeps its role of main tool to assess nerve function, but it provides functional data, while US supplies morphological information about nerves [1]. For this reason nerve US is increasingly becoming a routine technique in neurophysiology labs for the information that can add for diagnosis and therapeutic approach [1, 2, 7–9, 11].

US equipments are small devices, which can be taken to the patient's bedside, and they are much less expensive than other imaging systems. Examination time is very short and patient safety is guaranteed: there are no adverse effects nor contraindications, in fact it can be easily performed on children; moreover each body part can be assessed in every position with the possibility to perform dynamic scanning [2]. US can directly image nerves and demonstrate their internal structure consisting of several hypoechoic structures, the fascicles, embedded in a hyperechoic background, the epineurium [7]. The main limit of the US evaluation is the low ability to depict deep tissues.

Nerve US is a useful tool that provides important information in different peripheral nervous system diseases: entrapment neuropathies [7,9], traumatic nerve lesions [8], nerve tumors, and immune- mediated and hereditary neuropathies [10] are the conditions in which morphological information provided by US support the physician in diagnosis, prognosis, and treatment approach [4, 11].

Contributive role of ultrasound

In 2007 our group assessed the outcome of adding US to electrodiagnosis in patients affected by mononeuropathies and atypical clinical and neurophysiological presentation [7]. In these

conditions the combined use of electromyography (EMG) and US, performed in the same session was useful for diagnosis and determination of appropriate therapy. In an editorial on that study, Walker stated that by combining electrodiagnosis evaluation to US the approach to nerve and muscle diseases might be redefined [12].

In 2012 we demonstrated that the routine use of US in a neurophysiological lab could modify the diagnostic and therapeutic approach in a majority of cases [9].

In that study US impacted, namely modified the diagnostic and therapeutic path, in 42.3% of cases; US had a confirmatory role in 40%; US did not confirm clinical and neurophysiological diagnosis in 17.7%; no incorrect US findings were observed [9].

The contribution of US in traumatic nerve lesions (TNL) was assessed according to the previous classification, reported in our studies [7, 9], with some modifications to underline the more crucial role of US in those condition [8]:

• *Contributive:* when US findings enhanced diagnostic information, treatment, or follow-up.

• *Non contributive:* when US did not modify the diagnostic path or therapeutic strategies (even if diagnosis was reinforced by additional piece of evidence and information); this group included also cases in which US findings were normal.

Also in that study [8] US strongly modified the diagnostic and therapeutic path (in 58.0% of cases) providing information regarding therapeutic approach, diagnosis and follow-up (contributive group). In 42.0% of cases US findings were normal or confirmed clinical-neurophysiological results. So in these cases US did not modify the diagnostic path or therapeutic decision (non contributive group).

In TNL US contribution was particularly crucial (83.8% of the cases) in presence of complete axonal damage demonstrating the discontinuity of the nerve (neurotmesis) or continuity (axonotmesis). Moreover, in case of neurotmesis US was useful also to assess the distance between the nerve ends, presurgically providing data on the need of nerve graft and excluding neuromas or frayed nerve endings that surgically must be excluded. Concerning brachial plexus injury, that in our sample represented 16% of cases, it must be noted that US can provide only partial information because of blind tracts due to the clavicle, on the tract out of the spine. In these cases US may be useful but it cannot replace magnetic resonance imaging (MRI) that is crucial for assessing the roots avulsions that frequently occur in brachial plexus injury [8].

Intra- and internerve cross sectional area variability

Classically the quantification of nerve damage is reflected by the modification of Cross Sectional Area (CSA) [7–9, 11], a very useful measure especially in case of focal nerve damage. The role of US in the evaluation of polyneuropathies is still in its infancy and therefore not yet well defined, but roughly we can say that demyelinating polyneuropathies often present a diffuse or patchy enlargement of nerve CSA, whereas in case of axonal damage these findings are not commonly observed. This difference might be due to diverse pathophysiologic mechanisms underlying different neuropathies [3,13].

In fact, CSA alone cannot adequately quantify not homogeneous US alterations, such as those found in chronic immune-mediated neuropathies; the high clinical and neurophysiological variability is reflected in the US heterogeneity. Several reasons may account for the heterogeneity of nerve US findings, among which the high variability of the nerve disease, the fact that US evaluation is performed in different stage of disease and follow-up, and the possible role of therapy, that may modify disease activity and nerve appearance. In order to overcome the difficulty in quantifying the heterogeneity of US alteration, our group proposed two new US measures (intra- and inter-nerve CSA variability) [10] that might help to develop a scoring system necessary to compare data from different series and, in the same patient, to follow-up nerves modification. A limitation of these new measures is that they do not adequately assess US nerve variability at lower limbs. This is due to the current limited imaging capabilities of US and lower extremity anatomy (the deep location of the sciatic nerve and the short length of the fibular and tibial nerves).

Conclusions

The results of literature and of our studies [3, 4, 7–12] show that US could complement neurophysiological assessment in a consistent amount of patients with nerve impairment. The combined use of US and electrophysiology gives information that is impossible to obtain if we use neurophysiology or US separately [7,8,9]. In the light of the available data, US evaluation is absolutely recommended [2].

Nerve US has no risks in patients; it is able to evaluate the morphological relationships between nerve and other structures (anatomical or extrinsic) even in dynamic examinations.

The characteristics of US (quick, safe, painless and cheap) make it an ideal and adjunctive tool for the diagnostic work-up of neuropathies.

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Myosonology in Neuromuscular Disorders

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Key words:
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ultrasound

Recently the multimodal 2D/3D/4D myosonology has become the most appropriate non-invasive and bedside method for real time evaluation of structural and functional properties of the muscle tissue in normal and pathological conditions. Using high resolution B-mode ultrasound the physiological and pathological muscle structure and the positioning of needle electrodes for biopsy or injections (e.g., botulinum toxins or local anaesthetics) can be easily imaged. By tissue velocity imaging (TVI) the muscle motion can be better detected and quantified in terms of velocity, accelerations and synchronicity of muscle contraction. Using M-mode ultrasound different hand tremors can be recorded. Thus, the myosonology seems to become a powerful tool for neurologists and physiotherapists in their every day clinical practice.

Introduction

Myosonology is an alternative non-invasive imaging method for studying the muscle structure, nerves, bones, joints and their vascularization in healthy persons and patients with neuromuscular disorders. It gives unique opportunity of depicting in real time the functional muscle changes in rest, during voluntary, passive or electrically induced muscle contraction as well as to follow–up the spontaneous and/or therapeutically induced structural and functional muscle recovery [1, 14, 18].

Although good reliability of ultrasound muscle imaging has been proved by CT and MRI [15], its clinical application in neurology is still restricted mainly to particular research or treatment protocols.

Myosonology methods

At present, different ultrasound methods are used for structural and/or functional evaluation of muscles and nerves. Among them the ***B-mode imaging*** becomes a method of choice in clinical practices for non-invasive, easy and fast screening of normal or pathological muscles [15]. Generally, B-mode ultrasound pattern of each muscle includes hyperechoic epimisium (enveloping the whole muscle) and hypoechoic muscle fibers (grouped in fascicles and divided by hyperechoic septs of perimisium). ***Duplex scan*** (combination of B-mode with pulsed Doppler ultrasound) or ***B-flow imaging*** contribute to assessment of the arteries and veins of the skeletal muscles and the changes in their local blood circulation.

More detailed information for muscle architectonics can be obtained by using a ***four-dimensional (4D) ultrasound imaging***. It is based on the concept of combination of space and time in a single abstract "space“ with three spatial (length, width and height) and one temporal (time) dimensions. The ultrasound patterns reflect the degree of muscle atrophy, fat and fibrous tissue infiltration. This method, however, is not in routine usage because it is still expensive, needs a special probe and additional training [22].

Monitoring of velocity, acceleration and synchronicity of muscle contraction is another aspect of ultrasound investigation. Such information can be obtained by means of a ***Tissue Velocity Imaging (TVI)*** based on Doppler effect. By recording slow tissue movements during voluntary repetitive contractions in different muscle areas the kinetics of various muscle groups and fibers become visible. Hypo- or hyperkinetic zones, voluntary muscle movements, velocity of contraction and relaxation, repetition of movements, synergistic or dephasing (non-synchronous) muscle activity can be detected and quantified [19, 23].

Information about muscle motion over time can be obtained by ***M-mode ultrasound***. It gives temporal changes in echoes of the moving structures in which the depth of echo-producing interfaces is displayed along one axis (toward and away from the transducer) with time along the second axis. Although this method is commonly used in many fields of medicine (cardiology, angiology, etc.), its application in neurology is restricted predominantly to the monitoring of carotid artery motion and hand tremor frequency [25].

The combination of these methods improves significantly the diagnostic abilities of each particular method alone. Furthermore, the simultaneous application with electromyography (EMG) contributes for differentiation of primary muscle from peripheral

nerve damage. For correct diagnosis the history of the disease, the neurological status at the time of investigation and the experience of the investigator have also an important role.

Criteria for application

Myosonology is applied for clinical or research purposes by obtaining information for:

– Basic muscle anatomy – muscle location and structure (normal or pathological), visualization of partial or whole muscle atrophy, hypertrophy, degeneration or other changes in muscle architectonics, local circulation, nerves and surrounding tissue;

– Direct measurement of muscle size, longitudinal and transverse diameter in rest, during passive and active movement or electrical muscle stimulation (ES);

– Verification of specific inhibited or activated muscle fibers, spontaneous muscle activity, fasciculation or myoclonus;

– Estimation of the strength of muscle contraction by measuring the angle of inclination of the muscle fibers towards the surface of the aponeurosis in relaxed position, during active or passive muscle flexion/extension and ES;

– Imaging of the positioning of needle electrodes for biopsy or various injections (e.g., botulinum toxins or local anaesthetics);

– Better assessment of velocity, accelerations and synchronicity of muscle contraction during voluntary repetitive movements by Tissue Velocity Imaging (TVI) of muscle motion;

– Estimation of the degree of muscle atrophy, fat tissue infiltration and fibrosis;

– Estimation of the effects of therapeutic interventions (Botox or other type of injections);

– Differentiation of primary muscle from peripheral nerve damage using a simultaneous application of myosonology and electromyography (EMG);

– Determining the most appropriate areas for muscle biopsy (not too destroyed and not too preserved);

– Evaluation of functional muscle reorganization in presence of permanent neurological deficit;

– Testing the peripheral muscle pump efficacy in orthostatic intolerance;

– Testing the effect of drugs, rehabilitation approaches, training, etc.;

– Monitoring of hand tremors;

– Visual feedback for muscle re-education and muscle performance;

– Evaluating the impact of other co-factors (surrounding tissue, contractures, etc);

– Longitudinal follow-up in muscle degeneration or regeneration;

– Research purposes in clinical (in vivo) or laboratory (in vitro) settings.

Muscles are better evaluated in a lying position by using probes for 2D or 3D/4D real time imaging located at the anatomical place for each particular muscle. The longitudinal and transverse diameters, the angle of inclination of the muscle fibers towards the surface of the aponeurosis and, if possible, the 3D/4D muscle architectonics can be evaluated in rest, during passive, active or ES muscle movements. The results should be compared to mysononograms of age- and sex-matched healthy controls as no international reference values are available up to day.

Ultrasound patterns

The ultrasound patterns of muscle architectonics are relatively typical in normal and some pathological conditions. As general, they reflect the degree of muscle atrophy, fat and fibrous tissue infiltration.

Healthy subjects. The normal muscles are enveloped by hyperechoic epimisium. The muscle fibers are hypoechoic and grouped in fascicles, divided by hyperechoic septs of fibrous and fat tissue of the perimisium. In a longitudinal B-mode image the perimisium is depicted as oblique parallel hyperechoic lines (Fig. 1). As example, the plantar flexion (PF) of triceps surae muscle (TS) causes calf muscle contraction that increases the transverse muscle diameter and the

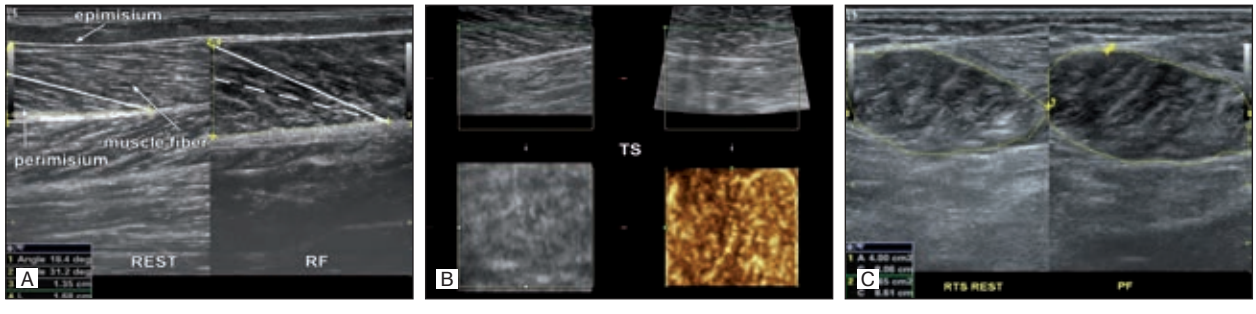

***Fig. 1. A**. B-mode image of TS muscle in rest and PF in a 27-year-old healthy woman. Dotted line presents the orientation of muscle fibers in rest. **B.** 3D/4D myosonogram with a reticular TS architectonics. **C.** Transverse diameter of TS muscle in rest and PF.*

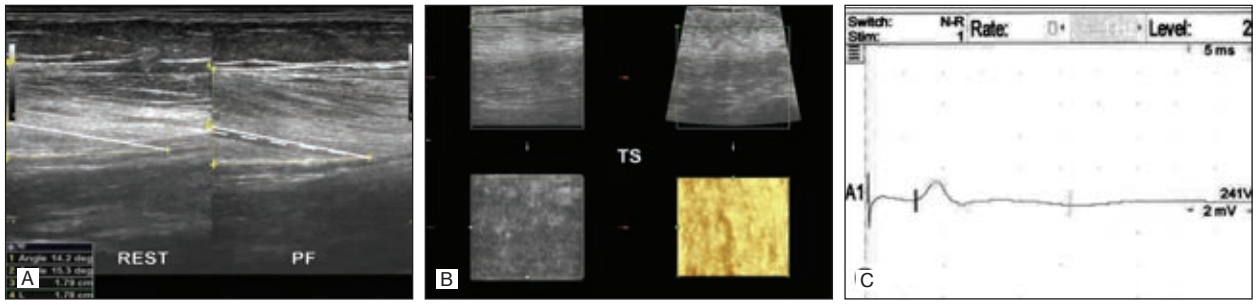

Fig. 2. A. *B-mode TS image in rest and during PF in the woman with genetic type of distal myopathy. Dotted line presents the orientation of muscle fibers in rest.* ***B.*** *Abnormal 3D/4D architectonics of the same muscle.* ***C.*** *Stimulation EMG revealed low amplitude and relatively normal motor latency [20].*

angle of muscle fiber towards the aponeurosis. The 3D/4D ultrasound imaging shows a reticular TS architectonics despite the muscle activity, age and sex of healthy controls. Its hypoechoic areas increase during PF, due to thickening of the contracted muscle fibers [16, 22].

Physiologically the skeletal muscles have a large adaptive potential as myocytes can adapt to different operational loads and conditions [9] – slow twitch muscle fibers (type 1) are rich in mitochondria and resistant to fatigue and fast twitch fibers (type 2) are less resistant to fatigue due to increased glycolysis processes, ensuring their energy [5]. In normal aging the number of muscle fibers decreases (sarcopenia) and the slow/fast muscle fiber ratio changes in favor to slow fibers. In active training, exercises or aging some physiological changes in muscle structure and muscle thickness can be established with ultrasound, but the reticular 3D/4D patterns continue to be preserved [22].

Distal myopathies (DM). They are a group of genetically and clinically heterogeneous disorders classified into one broad category, due to the presentation of weakness involving distal skeletal muscles of the limbs. Gene mutations encode different proteins that cause a progressive muscular dystrophy, followed by replacement of the normal muscle fibers with fibrous and adipose tissue [11, 12, 13]. These changes increase muscle echogenicity – the muscles become smaller and whiter in B-mode ultrasound imaging and with reduced muscle contractility. A combination of spot-like hypo- and hyperechoic areas has been reported with 3D/4D ultrasound imaging. The changes were associated with the degree of muscle atrophy, fat and fibrous tissue infiltration (Fig. 2) [20, 22].

Diabetic neuropathy (DN). It is a common late complication of diabetes, often manifested as a symmetric sensorimotor and autonomic neuropathy. Histological studies show neurogenic muscular atrophy with signs of chronic denervation and reinervation – angular small muscle fibers, muscle fibers type "target", grouping of muscle fibers in the form of bundle atrophy. The neurogenic damage of calf muscles are proved by different methods – clinical, neurophysiologic, neuroimaging, etc. [17]. The simultaneous usage of EMG and myosonography helps for evaluation of the severity of peripheral nerves damage and the changes in cross-striated muscles that could contribute to distinguish primary from secondary myogenic lesions in peripheral neuropathy [8]. Myosonographic patterns in low extremity neuropathy demonstrate bundle atrophy with mild to severe involvement of both lateral heads of triceps surae muscle, which correlates with the

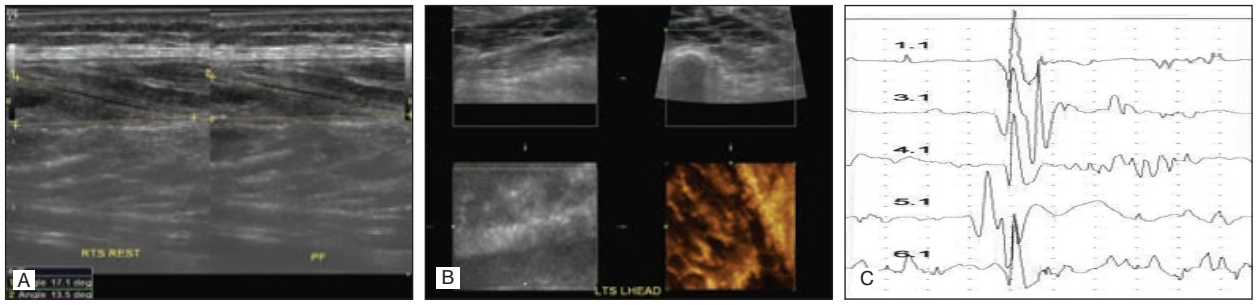

Fig. 3. A. *Triceps surae muscle myosonograms in diabetic neuropathy.* ***B.*** *Irregular strips hipoehoic strand type atrophy with reduced contractility of muscle fibers.* ***C.*** *Needle EMG showed polyphasic action potentials with higher amplitude and longer duration, fasciculations, fibrillations and positive sharp waves.*

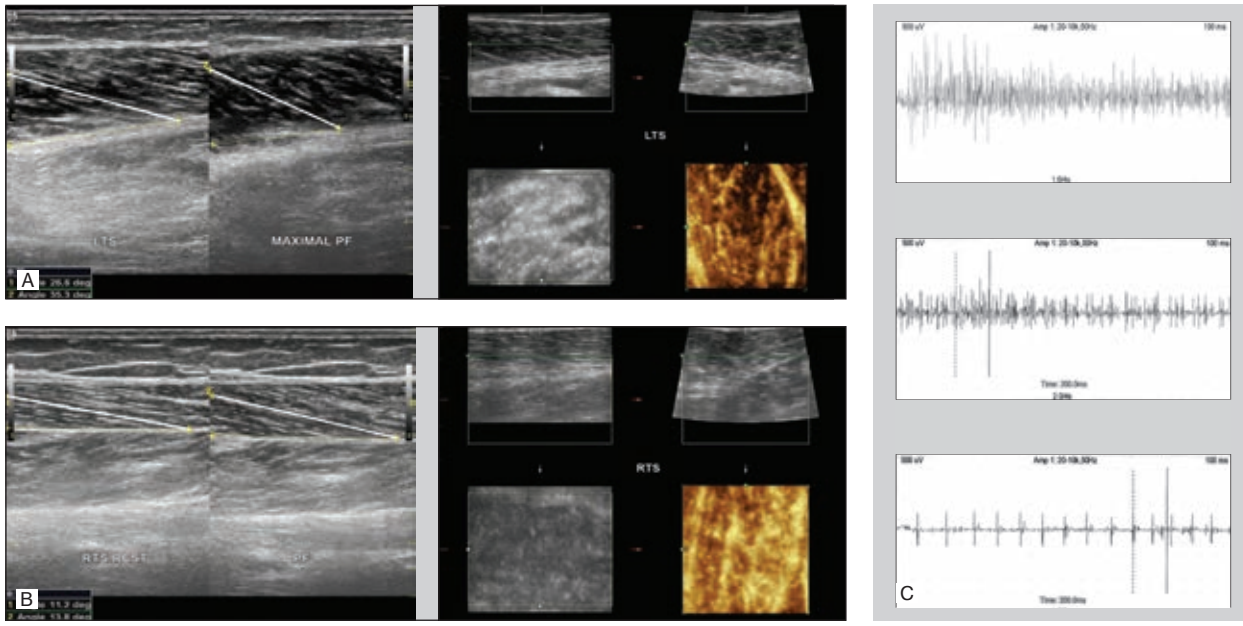

Fig. 4. *Myosonograms of m. triceps surae in a patient with post-stroke hemiparesis. Paretic leg* ***(B)*** *is with reduced volume and contractility of m. triceps surae compared to non-paretic side* ***(A)****. Compared to the controls (see fig. 1) bilateral changes in m. triceps surae myoarchitectonics are seen in stroke patient – fine reticular structure is replaced by more coarse granulated one, hyperechoic septa of perimisium fibrous and fatty tissue increase in size and number, significantly expressed on the side of paresis.* ***C.*** *EMG of TS at maximal contraction in a healthy control (top) non-paretic (middle) and paretic (bottom) leg. From the paretic muscle only single action potentials were detected. Compared to the control the non-paretic limb is with reduced amplitude of motor units action potentials and incomplete interference pattern at maximal contraction [21].*

histological evidence of neurogenic muscle atrophy (fig. 3). These finding differs significantly from the granular architectonics identified in genetic myopathies [6]. The clinical significance of myosonology as a method for early diagnosis, differentiation of neurogenic from myogenic muscular atrophy and longitudinal tracking of neuromuscular diseases evolution is subject to future studies.

Chronic hemiparesis after stroke. It has been demonstrated by different methods that in chronic unilateral stroke bilateral changes in motor control appear – the participation of the non-paretic side is proportional to the severity of brain injury and is associated with functional and structural changes in paretic muscles [7]. Unlike changes associated with normal aging, in paretic muscles an inactivity hypotrophy, accumulation of intramuscular connective tissue, increase of collagen/muscle ratio, fat accumulation, severe deficiency of slow myosin isoforms, shortening and relative atrophy of fast muscle fibers are seen [9], enhanced by physiological processes of aging. Changes in the non-paretic limb are also observed – reduced muscle strength at maximum contraction. By multimodal neurosonography bilateral asymmetrical changes in triceps surae muscle myoarchitectonics (on the paretic and non-paretic side) after stroke become visible – they can be assessed quantitatively and displayed structurally, which is essential for early diagnosis, selection and evaluation of the therapeutic approach (fig. 4). A decreased muscle volume of the paretic calf, asymmetric bilaterally enlarged hyperechoic septa of fibrous and fatty tissue in triceps surae perimisium and sonographic data for changed myoarchitectonics significantly expressed on the side of paresis have been reported – replacement of the normal grain grid structure of triceps surae muscle by a more coarse granular one, due to the inactivity hypotrophy, intramuscular connective tissue proliferation and fatty degeneration [21]. Using TVI non-synchronous muscle activity is also established on the spastic paretic side with reduced velocity of contraction, relaxation and repetition of movements. A significant decrease in contractility of the contralateral "healthy" side indicating a systematic slowing of movements in stroke patients is also seen. Furthermore, the US technique allows measuring of the kinetics of movements during disease progression and therefore it is ideal for monitoring exercise therapies or drug effects [23]. However, the application of myosonology in patients who have experienced stroke is mostly experimental.

Muscle injuries. Myosonology is a routine method in sport medicine and in traumatology – it is used in sportsmen and athletes to detect non-invasively muscle injuries like bleedings or disruption after exercise and give a prognosis of the healing process [2, 10]. The optimal time

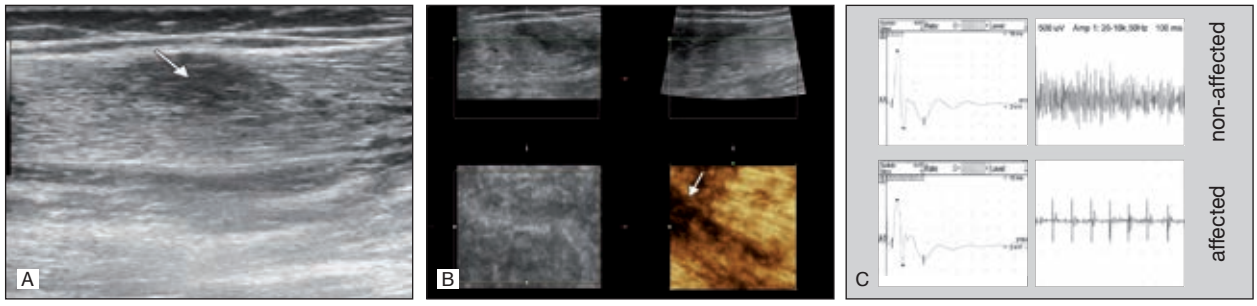

Fig. 5. *Traumatic TS lesion. Rupture of muscle fibers, intramuscular hematomas and perifocal muscle edema* ***(A, B)****. Pain induced limitation of muscle contraction during PF of the same muscle without changes in the angle of inclination to the aponeurosis.* ***C.*** *Stimulation of the tibial nerves and CMAP responses on the non-affected (up) and traumatic (down) TS muscles. The needle EMG showed a pain induced limited TS muscle contraction on the affected side. No EMG signs of peripheral nerve lesion bilaterally.*

window to survey muscle injuries is of 2-48 hours [3]. In clinical setting the myosonology contributes for fast diagnosis of any muscle fiber traumas, hematomas, pain due to vein dilatation, etc. (fig. 5).

Tremors. Recently, ultrasound M-mode tremorogram has been introduced as an alternative to EMG method for estimation of various hand tremors (parkinsonian, essential, psychogenic, etc.). A high coincidence of the tremor frequencies, measured by EMG and M-mode ultrasound, has been found. Both methods correlate entirely in measuring the tremor frequency before and after L-Dopa administration [25]. This examination is easy, fast and of low cost; it can be repeated many times and applied in patients with cardiac pacemaker without significant side effects. However, the M-mode ultrasound tremor recording gives reliable information only for the tremor frequency. No measurement of the pattern of flexor/extensor muscle activity is possible if only one probe is used (2 probes at the same time are needed). The measurement of the tremor amplitude is questionable and many artifacts could compromise the results. Therefore, the M-mode ultrasound monitoring can be used mostly as a screening method for differentiating of various hand tremors based on their frequency (fig. 6).

US guided EMG needle position, injections and biopsy. It has been shown that real time ultrasound muscle imaging facilities the needle EMG-examination in patients with muscle atrophy or obesity. An improved positioning and accuracy of the needles in the muscle can be achieved under ultrasound guidance [4]. The ultrasound resolution of the needle position is critically dependant on the needle diameter therefore fine electrodes will not be visualized. Due to movement artifacts of the needle in the ultrasound image and a re-assesment could be nessessary. Injection needles, especially when small air bubbles or liquid at the needle tip can be released enable a very accurate position identification [18].

The side effects of local injection of botulinum toxin for treatment of spasticity or dystonia can be avoided by B-mode guidance of the needle and

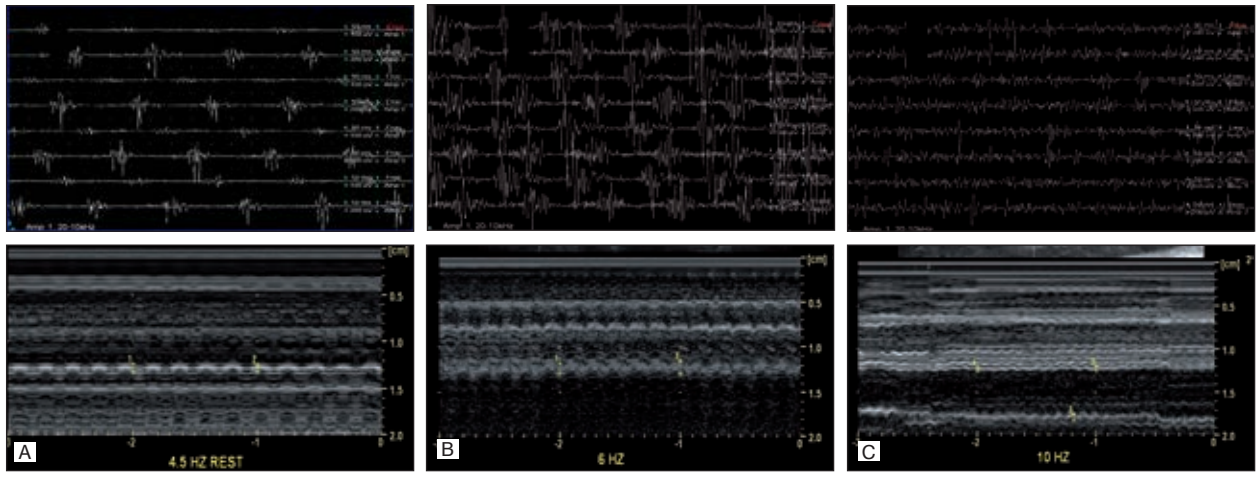

Fig. 6. *EMG (above) and M-mode (below) tremorograms in patients with parkinsonian* ***(A)****, essential* ***(B)*** *and psychogenic* ***(C)*** *hand tremor. There is a high coincidence of tremor frequencies, measured by both methods.*

volume injected into the right muscles or glands. By ultrasound control of the needle position injuries of adjacent blood vessels or surrounded tissue can be prevented. Verification of specific inhibited or activated muscle fibers is possible. Data are available for the anesthesia of the plexus, scalenus syndrome, and local anesthesia of n. obturatorius. Ultrasound B-mode imaging helps for determining the most appropriate areas for muscle biopsy (not too destroyed and not too preserved).

Fasciculation. As typical indicators for chronic axonal lesions they can be detected easily at the surface muscles. Their recognition can be difficult in obese patients or deeper muscle layers where B-mode imaging could help to detect smaller or slower spontaneous muscle movement, fasciculations or myoclonus [15, 18].

Neurorehabilitation. The application of myosonology in every day neurorehabilitation is still very restricted to: (a) estimation of muscle volume, degree of muscle atrophy and muscle fibre contractility before, during and after rehabilitation; (b) monitoring the muscle fiber kinetics during active or passive movements or EMG stimulation; (c) ultrasound navigation of needle positioning for botulinum injections; (d) testing the peripheral muscle pump efficacy due to orthostatic training; (e) evaluating the impact of other co-factors (surrounding tissue, contractures, etc) for peripheral nerve and muscle recovery; (f) clinical or experimental research for post-stroke brain reorganisation; (g) any morphological muscle changes that appear in time and their evolution [24].

Scientific research protocols. Myosonology is used alone or in combination with other diagnostic or therapeutic methods in different experimental research protocols in vivo and in vitro. So far, no multicenter trials in the field of neurology are published.

Conclusions

Myosonology seems to become a powerful tool for neurologists and physiotherapists in their every day clinical practice. The multimodal ultrasound imaging gives reliable non-invasive information for dimension, morphological changes and functional characteristics of the target muscle's areas in normal and pathological conditions. The myosonological patterns reflect the degree of muscle atrophy, fat tissue infiltration and fibrosis, which appear to correlate with the severity, the topic and the myoarchitectonics of muscle lesion. However, why and when to apply myosonology for clinical usage depends on the level of competency (technical and human resources) of each laboratory and the purpose of the particular research protocol. Further multicenter trials are needed to establish international guidelines for application of myosonology in the field of neurology and related neuromuscular disorders.

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Ultrasound Imaging of Neck Muscles for Botulinum Toxin Injection

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Key words:
botulinum toxin, cervical dystonia, needle navigation, placement, ultrasound-guidance, ultrasonography

Botulinum neurotoxin (BoNT) injection has been increasingly used for treating muscular spasticity and dystonia. Unlike other techniques of precision targeting such as electromyography or computed tomography that have been described to minimize undesirable BoNT effects, B-mode ultrasound allows immediate and high-resolution imaging of the injection needle position within the target region. Visual identification of muscles and depth control of needle placement are the key features of ultrasound-guided injection that lead to improved targeting and safety of BoNT injections. Ultrasound may be helpful to validate already established injection techniques or when learning the correct injection technique. Ultrasound-guided BoNT injection has been recommended as a standard procedure in treatment of lower leg spasticity in children with cerebral palsy. In recent years, this technique has been increasingly used also for the exact targeting of BoNT injection in patients with cervical dystonia. The ultrasound-guided BoNT injection is especially recommendable if the scalene muscles; the longus colli, longisslimus capitis, or the obliquus capitis inferior muscles are targeted. The upcoming MRI-ultrasound fusion imaging techniques that are available already today with advanced ultrasound systems allow the ultrasound-guided targeting also of small deep muscles such as the longus colli muscle in patients with antecollis.

Clinical applications

Botulinum neurotoxin (BoNT) therapy is used in neurology to treat muscle hyperactivity disorders including dystonia, spasticity, cerebral palsy, hemifacial spasms and re-innervation synkinesias. For an optimal effect exact BoNT placement in the target muscle is important. Ultrasonography (US) allows non-invasive, real-time imaging of muscles and their surrounding structures. US can therefore visualise and guide the entire procedure of BoNT application [6, 7]. The results of several studies suggest that US-guidance can improve efficacy and reduce adverse effects of BoNT therapy when compared to conventional placement [1–5]. In task-related dystonia such as writer's cramp and musician dystonia the importance of exact targeting by US is especially high because (i) only the functionally relevant muscle should be weakened and (ii) only small quantities of BoNT can be injected since otherwise functionally relevant paresis can occur [2]. Compared to EMG-guidance US-guidance allows a more precise placement of BoNT in the target muscle, especially in small muscles. In the neck region US-guidance is recommendable in patients with cervical dystonia when the anterior or middle scalene, longissimus capitis and the obliquus capitis inferior are target muscles [6, 7, 8]. The exact knowledge of the muscular anatomy including its display on ultrasound and training of eye-hand coordination are prerequisites for the US-guided approach. If US-guided BoNT injection is adequately performed the results are a stable therapeutic response and often the need of lower BoNT doses compared to the visual approach of BT injection. An interesting novel approach for selected patients is ultrasound-MRI real-time fusion imaging to target BoNT injection into very deep muscles [7].

Method

Ultrasound machines used for BoNT application are the same as those used for vascular US. In principle, all contemporary US machines can be used if equipped with an appropriate linear-array transducer. The applied US frequency determines both the image resolution and the penetration depth. Increasing frequencies increase image resolution, but reduce penetration depth and vice versa. Superficial and small target muscles require optimal resolution and therefore higher US frequencies of about 13.0 (10-18) MHz. Profound and large target muscles in the neck, trunk and leg can be visualised also with lower US frequencies of about 7.5 (5-10) MHz. BoNT injections are usually performed with 20 mm,

27-gauge (outer diameter: 0.40 mm) needles or 40 mm, 27-gauge needles. For profound muscles an 80mm, 23-gauge (0.60 mm) needle may be used. Skin disinfection should be performed with non-alcoholic agents since alcohol may harm the US transducer surface. Then the injection needle is inserted adjacent to the US transducer. In principle, there are two techniques of US-guided needle insertion with respect to US imaging plane: the in-plane technique and the off-plane technique. The "freehand" off-plane technique is sufficient for most applications of US-guided BoNT injection. For this, the US transducer should be placed in a way that the target structure is displayed in the centre of the US screen. Then the midpoint of the transducer length corresponds to the location of the target structure and can be used as landmark for needle insertion. The inserted needle is displayed with high echogenicity with its intensity depending on the needle size. The injected BoNT solution usually presents as weakly echogenic depot leading to a local volume increase of the injected muscle.

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Burning Mouth Syndrome – Recent Concepts

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Key words:
burning mouth syndrome,
classification,
clinical presentation,
definition,
psychiatric comorbidity

According to International Headache Society (IHS) classification, burning mouth syndrome (BMS) is intraoral burning sensation without obvious medical and dental cause. IHS diagnostic criteria of the disorder include the presence of burning oral sensation during the most of the day without obvious changes of oral mucosa. Local and systemic causes have to be excluded by appropriate diagnostic procedures. Subjective feeling of dry mouth, paraesthesias and taste changes could be associated symptoms.

Estimated prevalence of BMS in general population varies between 1 and 15% and the disorder is seven times more common in females.

This condition is probably of multifactorial origin, often idiopathic, and its etiology remains largely obscure. BMS represents a disorder with a very poor prognosis in terms of quality of life, and the patient's lifestyle may worsen when psychological dysfunctions occur. As a result, BMS subjects continue to be high consumers of healthcare resources.

More recently, increasing attention has been given to the altered perception of sensory functions as well as to the changes in the psychological profile of many BMS patients. As a result, both disturbances should be included in the clinical spectrum of BMS.

BMS is primarily characterized by burning and/or painful sensations of the mouth with no mucosal lesions or any other clinical signs. It can occur at any site within or surrounding the oral cavity.

As in the other chronic pain conditions it has been reported that depression and anxiety are strongly associated with BMS and that they are significantly more frequent in BMS patients.

Introduction

According to the International Classification of Headache Disorders (IHC), burning mouth syndrome (BMS) is an intraoral burning sensation for which no medical or dental cause can be found [1]. BMS, coded 13.18.5, is classified in IHC as a separate group with other cranial neuralgias and central causes of facial pain [1].

Diagnostic criteria include: [1]

A. Pain in the mouth present daily and persisting for most of the day

B. Oral mucosa is of normal appearance

C. Local and systemic diseases have been excluded

- Pain may be confined to the tongue (**glossodynia**).
- Subjective dryness of the mouth, paraesthesia and altered taste may be associated symptoms.

Epidemiological studies have estimated BMS to be prevalent in 1–15% of the general population; the disorder is seven times more common in females than males [2].

The prevalence of BMS reported from international studies is from 0.7 to 4.6%. The mean age of BMS is between 55 and 60 years, with occurrence under 30 being rare. The ratio between females and males varies from 3:1 to 16:1. Furthermore, up to 90% of female patients with BMS are perimenopausal, with typical onset from 3 years prior to 12 years post the beginning of menopause. Despite the large number of clinical and epidemiological studies, pathogenesis and aetiology of BMS remains unclear [3]. Recent clinical, electrophysiological [4, 5] and histological [6] studies suggest that primary neuropathic dysfunction might be involved in the pathogenesis of BMS. On the other hand, a central mechanism with the involvement of dopamine receptors in the basal ganglia was suggested to play a role in the pathogenesis of the disease [7]. Recently, we published data based on decreased calcitonin gene-related peptide levels in saliva of BMS patients, showing that trigeminal nerve degeneration may be the underlying cause of BMS [8].

The possible theories behind the cause of BMS are [2-9]: 1) Abnormal interaction between the sensory functions of facial and trigeminal nerves. According to this theory, certain individuals labeled as supertasters (mainly females) due to the high density of fungiform papilla present on the anterior aspect of tongue, are at risk of developing burning pain; 2) Sensory dysfunction associated with small and/or large fiber neuropathy; 3)

Centrally mediated alteration in the modulation of nociceptive processing. This theory explains the fact that resulting in reduced central pain suppression in BMS individuals; 4) Disturbances in the autonomic innervation and oral blood flow; 5) Chronic anxiety or stress results in the alteration of gonadal, adrenal, and neuroactive steroid levels in skin and oral mucosa.

Psychological factors are, however, frequently associated with BMS. Previous studies have shown that diagnoses such as depression, generalized anxiety, hypochondriasis, and cancer phobia are often represented in patients with BMS [9]. It has been reported that depression and anxiety are strongly associated with BMS and are more frequent in BMS patients than in non-BMS subjects [10-13]. In contrast to this correlation, some authors assert that higher levels of anxiety and depression can be the consequence of chronic pain of BMS [14].

This chronic pain syndrome mainly affects middle-aged women with hormonal changes or psychological disorders. BMS is probably of multifactorial origin, often idiopathic, and its etiopathogenesis remains largely obscure. BMS represents a disorder with a very poor prognosis in terms of quality of life, and the patient's lifestyle may worsen when psychological dysfunctions occur [15]. Despite the fact that a voluminous amount has been published in this field, an universally accepted definition of this syndrome is still lacking. Various synonyms, such as stomatopyrosis, glossopyrosis, stomatodynia, glossodynia, sore mouth, sore tongue, and oral dysesthesia, have been adopted to emphasize the quality and/or the location of pain in the oral cavity. In this syndrome, however, pain represents the main symptom within a variety of chronic oral complaints. Thus, BMS appears to be the most appropriate terminology. Despite this large body of evidence, some issues on BMS are still debated, and they present a challenge for both researchers and clinicians. What generates a major dilemma is that BMS is defined by symptoms that can potentially arise from numerous different local/systemic pathologies, some of which can be clearly identified and managed, and others that elude diagnosis and, thus, hamper management [15]. Several authors [16, 17] have focused their efforts on establishing whether BMS should be considered as a distinct "syndrome", or it mostly represents a "symptom disruption" for a large number of conditions arising from a wide array of pathologies (hormonal changes, nutritional deficiency, etc.). They have proposed the lack of local/systemic factors as inclusion criteria for a "true BMS", and assumed that all the other types of "unremitting oral burning" correlated to different pathologies may be one symptom within the clinical spectrum of such a group of pathologies. Burning pain without mucosal or skin lesions, however, represents the typical symptom of chronic neuropathic pain conditions resulting from nerve damage, and in recent years a neuropathic basis of BMS has been better identified through the use of more sensitive diagnostic techniques [18]. This new evidence, in increasingly larger groups of BMS subjects, suggests a common background of neuropathy in the pathogenesis of this syndrome. As a result, it seems more appropriate to recognize two clinical forms of BMS: *"Primary BMS"*, or essential/idiopathic BMS for which organic local/systemic causes cannot be identified; and *"Secondary BMS"*, resulting from local/systemic pathological conditions and thus potentially sensitive to etiology-directed therapy. According to these criteria, "idiopathic" BMS as well as the "secondary" form may represent two distinctive subgroups of the same "pathological entity" [15-18].

A. Classification of the BMS types and subtypes

According to potential associated etiologies, BMS may be divided into *primary* and *secondary* types. Primary type includes idiopathic, non-neuropathic BMS. *Burning mouth sensations* (formerly, *secondary* BMS) are associated with established organic/therapeutic-related etiologies (e.g., oral cavity disorders, including oral local neuropathy, systemic disorders, nutritional deficiencies, drug-induced, neurological and psychiatric abnormalities) [19].

Burning mouth sensations are symptoms of these alterations and according to available literature, do not represent a distinct type of BMS. The latter starts with a differential diagnosis based on the exclusion of both other orofacial chronic pain conditions and painful oral diseases exhibiting mucosal lesions. The co-occurrence of overlapping/overwhelming oral mucosal pathologies, such as infections, may cause difficulties in the diagnosis and it is classified as *"complicated BMS"* [19].

Burning mouth syndrome has been further divided into three subtypes based on the daily variation of symptoms [19]: *Type I BMS* refers to complaints of burning sensation every day, that is not present in the morninig on awakening but develops later during the day, being maximal in the evenings. *Type 2 BMS* (the most frequent subtype; relative frequency: 55%) is characterized by constant burning pain all day, every day. The patients with Type 2 BMS tend to be most resistant to therapy. In type 3 BMS (relative frequency about 10%) pain is present intermittently on some days with pain-free intervals and affects unusual sites, such as buccal mucosa or the throat. Nonpsychiatric factors have been linked with Type 1 BMS, psychiatric factors, especially

chronic anxiety with Type 2, and food additives or flavoring allergies, with Type 3 BMS [19].

Clinical presentation

BMS is dominantly characterized by burning and/or painful sensations of the mouth with no mucosal lesions or any other clinical signs. It can occur at any site within or surrounding the oral cavity. The most frequently affected site is the tongue, in particular the tip and anterior two thirds, followed by the lower lip and hard palate [15, 19].

The pain in BMS is experienced as quantitatively similar to, but qualitatively different from toothache pain. BMS can be considered as a chronic pain syndrome with symptoms usually lasting for several months to several years [15]. Oral burning is most prevalent in postmenopausal women; figures of up to 40% have been presented. The prevalence of prolonged oral burning of BMS patients is about 8% with less than 1% suffering from continuous burning symptoms [15, 18]. The term BMS clinically describes a variety of chronic oral symptoms (Table 1) that often increase in intensity at the end of each day, and that seldom interfere with sleep [15]. Accordingly, two specific clinical features define this syndrome: (1) a "symptomatic triad", which includes unremitting oral mucosal pain, dysgeusia, and xerostomia; and (2) "no signs" of lesion(s) or other detectable change(s) in the oral mucosa, even in the painful area(s) [15].

In the remaining cases, "oligosymptomatic" (pain and dysgeusia or pain and xerostomia) or "monosymptomatic" (pain only) forms of BMS are the most frequent presentations.

More recently, increasing attention has been given to the altered perception of sensory/chemosensory functions as well as to the changes in the psychological profile of many BMS patients. As a result, both disturbances should be included in the clinical spectrum of BMS [18]. Oral pain represents the cardinal symptom of BMS. The type of pain experienced by BMS patients is a prolonged "burning" sensation of the oral mucosa. However, scalding, tingling, or numb feelings of the oral mucosa have also been reported [15-19].

The onset of oral pain is generally spontaneous and without any recognizable precipitating factors. Some individuals with BMS relate the onset of pain to previous events such as dental procedures (particularly dental extractions, dental prostheses) or other disease [15].

Psychiatric comorbidity

Personality and mood changes (especially anxiety and depression) have been consistently demonstrated in patients with burning mouth syndrome and have been used to suggest that the disorder is a psychogenic problem. However, psychological dysfunction is common in patients with chronic pain and may be the result of the pain rather than its cause.

Concerning the association between BMS and psychiatric diseases, an extensive literature, varying from anecdotal reports, psychoanalytic opinions, and controlled comparisons to large-scale surveys, attests to the importance that is generally assigned to the relationship between psychiatric disorders and BMS. Despite different methodological approaches and sometimes, small study groups, all of the studies reported a high prevalence of psychiatric symptoms or of mental disorders. About 50% of the cases of BMS are comorbid with other current psychiatric disorders [20]. There has been particular emphasis on depression [21], chronic anxiety [22], cancerophobia, and hypochondriasis [20]. The association of psychiatric disorders, fundamentally depression and anxiety, with BMS has often been reported in the literature. As a result, some authors have suggested a psychosocial cause for BMS [20, 23].

Table 1. Main symptoms in patients with BMS

Symptom	Type(s) of Complaint(s)
Oral mucosal pain* (main complaint)	Burning Scalding Tingling Numb feeling
Dysgeusia*	Altered taste perception
Xerostomia*	Dry mouth
Others	Thirst Headache TMJ pain Tenderness/pain in masticatory muscles, neck, shoulder, and suprahyoid muscles

** BMS symptomatic triad; TMJ = temporomandibular joint.*

Although there is widespread agreement over the participation of psychosocial aspects in the cause of this disorder, current thought is that multiple factors are involved [20-23].

However, when reviewing the literature, it is interesting to note that anxiety and depression are the two psychopathologic factors in BMS that have almost exclusively been evaluated by questionnaires. The situation of these patients in other psychopathologic contexts is somewhat uncertain, although recently a number of studies have addressed the subject [20].

High frequency of somatic reactions to stress was observed in a series of 154 patients with BMS. The preoccupation of these patients with their physical condition and bodily functions constitutes a further feature of BMS with hypochondriac reactions [24].

In the study of Lamey and Lamb (25) the majority of the 75 patients studied were female, which agrees with previous studies relating to burning mouth syndrome. Analysis of the Hospital Anxiety and Depression (HAD) scale completed by the patients in this study showed that 39% had clinically significant anxiety, 23% had anxiety scores of borderline significance and 38% were not anxious. The depression subscale presented very different score ranges, with 13% indicated as having depression, and 68% having scores that corresponded to a non-depressive state; 19% had results of borderline significance [25]. From the results of this study it could be concluded that more than one third of the BMS patients, the majority of whom were female, had anxiety. This suggested that their somatic symptoms of burning mouth were at least partly the psychological result of restlessness, tension, and an inherent inability to relax [25]. Only one in seven patients in this cohort had depression, suggesting that depression does not seem to play an important role in the etiology of burning mouth syndrome as previous publications suggested [25].

From the psychiatric and psychopathologic viewpoint, two groups of patients with BMS may be distinguished: with or without associated psychiatric symptoms. No psychopathologic phenomenon was detected that was common to all patients with BMS and that differentiated them from controls free of oral symptoms. The association of BMS and psychological changes might be a mere coincidence, although the high percentage of persons with BMS who have these alterations (about 50%) compared with the general population would seem to disprove this.

BMS patients may be particularly vulnerable to psychiatric problems, primarily depression and anxiety. Such comorbidity could be mediated by many factors, including those of psychological nature, particularly in persons suffering chronic pain condition or other psychological triggering factors [20-22].

Consideration should also be given to other possible explanations for the association between BMS and depression or anxiety disorders, including the possibility that both aspects might be the product of a common factor.

Observed higher incidence of these alterations among postmenopausal women points to an endocrine disorder as the underlying cause of both the oral and psychopathologic symptoms.

The most commonly observed association is between BMS and depressive and anxiety symptoms. The items on the anxiety and depression scales tend to exhibit marked correlations to the point of rendering it empirically impossible to develop independent subscales of these two psychopathologic entities [21, 26].

Management

The treatment of BMS is usually directed at its symptoms and is the same as the medical management of other neuropathic pain conditions [27]. The first step in management is contingent on the specific type of BMS, primary versus secondary. The goal of therapy for secondary BMS should initially be directed at treating the causative local or systemic disease and withdrawing offending medications (such as ACE inhibitors). This etiology-directed therapy typically yields a good response. The cure for primary BMS, however, remains elusive despite attempts with different classes of medication. The variable response rate to medical therapy is likely due to the multifactorial pathophysiology of idiopathic BMS, including irreversible processes.

Investigated strategies include benzodiazepines, antidepressants, topical capsaicin, alpha-lipoic acid, hormone replacement therapy, vitamins, anticonvulsants, biofeedback technique to modify parafunctional habits, and psychosocial therapies. As an adjunctive therapy method, acupuncture is referred to in the art as being beneficial for the relief of symptoms in patients with BMS. Studies generally support the use of low dosages of clonazepam [28], chlordiazepoxide [29] and tricyclic antidepressants [30]. Evidence also supports the utility of a low dosage of gabapentin [31]. Studies have not shown clear benefit from treatment with selective serotonin reuptake inhibitors or other serotoninergic antidepressants [27]. Although benzodiazepines might exert their effect on oral burning by acting as a sedative-hypnotic, this possibility appears to be unlikely because the maximal effect of clonazepam is usually

observed at lower dosages [27]. The beneficial effects of tricyclic antidepressants in decreasing chronic pain indicate that, in low dosages, these agents may act as analgesics [27, 30]. Topical capsaicin has been used as a desensitizing agent in patients with burning mouth syndrome. However, capsaicin may not be palatable or useful in many patients [32].

Additionally, modifications of parafunctional habits may offer some symptom relief. Tongue protectors (worn 15 min three times a day) were shown to significantly improve pain scales in BMS patients after two months of treatment, however sample sizes were small and placebo effect could have been introduced [27, 28].

Conclusion

BMS is a relatively common chronic intraoral pain disorder classically characterized by intractable burning that may be associated with dysgeusia and xerostomia. Etiology of BMS is multifactorial, and a secondary form of BMS should be diligently sought for and properly treated. Multidisciplinary approach including medical and psychosocial therapy may be effective in symptom relief in patients with BMS.

Further studies are necessary to establish long-term prognosis. BMS remains an important medical condition, which often places a significant burden on the patient and healthcare system and requires adequate and timely recognition and treatment.

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Home-based Neurorehabilitation in Diabetic Neuropathy

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Key words:
diabetes mellitus,
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orthostatic reactivity

Diabetic neuropathy (DN) is one of the most common complications in patients with diabetes mellitus type 2. It affects from 22.5% to 28.5% of all diabetic patients worldwide; on national scale the morbidity reaches 50-70% of the affected patients.

Neurorehabilitation is one of the main therapeutic approaches in the whole algorithm of treatment of DN. The ability to perform long-term, specialized physical therapy at home is essential for patients with chronic neurological deficits. For this reason, we offer diabetic neuropathy patients the possibility of metabolic control, symptom reduction and orthostatic improvement through systemic self-fulfillment of purposeful physical exercises. Increasing their daily motor activity will improve their self-esteem and quality of life.

Diabetes mellitus is the fourth leading cause of global death by disease. More than 246 million people suffer from diabetes worldwide with a tendency this incidence to rise to 380 million by 2025. The disease is associated with an increased relative risk for ischemic stroke, ischemic cardiac disease, chronic insufficiency of the lower extremities and chronic microvascular complications as retinopathy, nephropathy and neuropathy [19].

Diabetic neuropathy (DN) is the most frequent complication. It affects 22,5% то 28,5% of all diabetic patients worldwide, and on national scale the morbidity reaches 50-70% of the affected patients [14]. The feet and legs are often affected first, followed by hands and arms. Signs and symptoms of peripheral neuropathy are often worse at night, and may include: numbness or reduced ability to feel pain or temperature changes; a tingling or burning sensation; sharp pains or cramps; increased sensitivity to touch for some people, even the weight of a bed sheet can be agonizing; muscle weakness; loss of reflexes, especially Achilles'; loss of balance and coordination; serious foot problems, such as ulcers, infections, deformities, and bone and joint pain [12].

Neurorehabilitation

Neurorehabilitation is one of the main therapeutic approaches in the whole algorithm of treatment of DN. It studies and applies complex medical approaches for compensating the damages of the nervous system, offsetting the emerging functional impairments and changes in the lifestyle of the patient and his family. By supporting and restoring the independence, self-confidence and positive mood of the patients, it helps their adaptation and successful reintegration into society.

Contemporary neurorehabilitation is defined as: holistic – positively influences the physical, cognitive, psychological and social dimensions of personality and enhances the quality of life of the patient and his family; individual, intensive and specifically focused – individually tailored and focused on the needs of the patient; planned – structured and performed by a multidisciplinary team of highly qualified and motivated professionals; cooperative – realized with the active participation of the patient and his family members; continuous – ensuring care, tailored to the needs of the patient throughout his life to restore and influence early and late complications of the disease; social – establishes appropriate community conditions aiming partial or complete re-socialization of the patient [23].

In the case of peripheral nervous system damage neurorehabilitation influences the segment reflex arc and the secondary complications through: positive impact on the superficial and deep sensation through stimulating of vasodilatation and improving tissue trophic and metabolism [15]; improved muscle strength and blood flow to the tissues, optimizing the oxygen and metabolic needs of the body when loading is intense and a series of repeated exercises against resistance is performed [26, 32]; restoration of coordination and balance by influencing proprioception by coordination exercises with and without visual

control [4]; improved orthostatic autoregulation by stimulating proprioception, activation of the sympathetic nervous system and increase of the efficiency of the muscle pump (increased muscle strength of the lower limbs, positional and cardiovascular training) [5].

Physical therapy

Physical therapy (PT) is a major part of neurorehabilitation. According to available literature concerning physical activity in patients with diabetes type II, the metabolic effect of therapeutic exercises depends on the their duration and intensity. Mild and moderate intensity has been shown to improve the three-phase process of better absorption of muscle glycogen, blood glucose and free fatty acids. A 40-60 min physical therapy program is recommended in the patient's daily life, producing real opportunities to reduce hyperglycemia. The reason for this is the fact that in the first minutes of exercising, the main source of energy is muscle glycogen, and the rate at which the glycogenolysis occurs in muscles, is highest in the first 5-10 min. In the subsequent physical effort (between 10 and 40 min) is the peak stage of glucose uptake in the tissue cells. Then follows a period during which glucose degradation begins to decrease and an increased (up to 70%) use of free fatty acids is involved, which leads to favorable changes in the lipid metabolism [2, 11, 37]. The American Diabetes Association (2001, 2003) demonstrates the beneficial metabolic effect that can be maintained for at least 5 years with regular exercise 3-4 times per week with an intensity of 50-70% VO2 max and duration of training 30-60 min [34]. According to Ohtsuka et al. (1998), daily walking of 3 km and 8 km significantly reduces the blood sugar level by 39.7%, regardless of the distance.

Sensory disorders cause an impairment of the coordination and balance of patients with DN, related to the high risk of traumas and injuries, especially of the lower limbs, which significantly obstructs the daily activities and the gait [33]. A number of authors recommend a precise PT approach in patients with DN and sensory impairment [26]. It requires the exclusion of exercises that increase plantar tension (walking without orthopedic shoes, running and static loads). Sports such as swimming, cycling and rowing are considered appropriate [28, 36].

A major problem with patients with DN is the motor dysfunction. A study on the strength of extensors and flexors of the knee and ankle joints found that muscle weakness was linked to the severity of neuropathy and disturbed the pattern of walking of the patients [29]. To improve muscle strength, in the PT practice exercises against resistance are recommended, resulting in an increase of the muscle strength from 30 to 100%, with intensity of 80% of the maximum aerobic capacity, and performing 2-3 sets of 8-10 repetitions for every exercise, three times a week [16, 32].

In patients with DN, balance is impaired as a result of sensory disturbances that are largely offset by the visual analyzer and impaired biomechanical balance factors (center of gravity, line of gravity, weight-bearing area and stability limits), due to muscle weakness in the distal parts of the lower limbs, decreased movement of the ankle joint and pain [17]. Based on the indicated static balance disturbances, the principal recommendations for PT effect on sensory ataxia in neuropathy are aimed at improving proprioreception by excluding or destabilizing the visual analyzer when the patient is standing on a solid basis [9].

In patients with DN and orthostatic dys-autoregulation, orthostatic hypotension is present and therefore many authors recommend physical activity with moderate intensity according to the insulin intake (which has a direct vasodilatating effect on peripheral blood vessels and may aggravate the present hypotension) [10].

Specialized physical therapy

For practice we have developed a substantial and augmented specialized physical therapy, suitable for application in clinical conditions, which is adapted for home usage as a home based self-directed learning didactic tools for rehabilitation. The program is easy to perform for a long time and increases the activities of daily living in patients with DN [3, 4].

The proposed 39 self-directed learning didactic tools are specialized physical therapy with a 45-minute duration and moderate load intensity. The introduction part of the exercise complex aims to adapt the cardiovascular system in a gradual manner (thoracic and diaphragmal respiration, rhythmic exercises of distal muscle groups, isometric exercises in circulatory regimen). The essential part of the physical therapy methods aims to increase muscle strength (by means of exercises against determined dose resistance, defined by elastic bands Thera-Band), and improve the sensitive, coordination and balance abilities of the patients (by means of targeted exercises). The final part of the complex includes autogenic training for general relaxation of the patient.

To objectify its effect we have studied 124 patients suffering from diabetic neuropathy and

Table 1. Changes in the muscle strength, the girt of calves and mobility of ankle and knee joint

Parameter	Group	Beginning (EG=48; CG=34) $\bar{X}\pm S_D$	On the 10th day (EG=90; CG=34) $\bar{X}\pm S_D$	On the 6th week (EG=90; CG=34) $\bar{X}\pm S_D$	On the 6th month (EG=90; CG=34) $\bar{X}\pm S_D$
Manual muscular testing of dorsal flexors (degrees)	EG	4.58±0.50	4.82±0.38***	4.96±0.21***	5.00±0.00***
	CG	4.74±0.45	4.74±0.45	4.62±0.49*	4.53±0.51*
	p	0.108	0.283	**0.001**	**0.001**
Girt of the calves (cm)	EG	37.60±2.51	38.03±2.52***	38.50±2.46***	38.52±2.20***
	CG	39.51±1.83	39.46±1.96	39.35±2.05	38.53±2.09***
	p	**0.001**	**0.004**	0.075	0.466
Speed of movements in the knee joint (s)	EG	22.00±2.70	18.51±2.57***	16.84±2.56***	17.78±2.76***
	CG	21.76±6.60	20.94±5.67	22.00±7.04	25.35±3.26***
	p	0.778	**0.001**	**0.001**	**0.001**
Speed of movements in the ankle joint (s)	EG	19.84±4.04	15.84±3.36***	14.56±3.34***	15.00±3.06***
	CG	18.97±4.76	19.21±3.41	19.88±3.00**	22.65±2.77***
	p	0.355	**0.001**	**0.001**	**0.001**

*$\bar{X}$ – average values of the studied parameters; S_D – standard deviation; ***p<0.001, **p<0.01, *p<0.05 – considerable differences for each group in the course of treatment with respect to initial values; p-considerable differences between the experimental group (EG) and the control group (CG); The obtained results were processed statistically using Wilcoxon test (in order to determine the importance of changes from manual muscular testing for each group in the course of treatment), the U-criterion of Mann Whitney (in order to be determined the importance of differences between the two groups from manual muscular testing) and Student t-test for the remaining indicators.*

diabetes mellitus type 2, divided into two groups. The experimental group includes 90 patients (52 women and 38 men, average age 58.47±8.69 years); the control group consists of 34 patients (16 women and 18 men, average age 58.79±7.49 years). The patients from the experimental group were included in a 6-month specialized physical therapy after a given written informed consent for long-term performance of therapeutic exercises at home. The control group patients were treated routinely using the standard 10-days physical therapy applied only during their in-hospital stay.

The specialized physical therapy ensures long term positive effect on patients with DN. Its prolonged and systemic application improves the carbohydrate and lipid metabolism of the patients. It mobilizes the local blood circulation and works against the main damaging factor – hyperglycemia, which is connected to better functional status of the peripheral nerves [4, 18].

It was proven that physical therapy has positive influence on the current neuropathic symptoms (sensory, motor, balance and changes in the peripheral conductivity). In order to influence positively the symptoms, it is appropriate to apply physical activity without using the body weight – resistance exercises (elastic Thera-Band stripes applied in 2-3 series of 8-10 repetitions each, at least 3 times a week) and post-isometric relaxation. Walking should be performed with silicon footpads, with and without eye control [9, 20].

The objective changes in muscle strength, muscle mass and the mobility of lower limbs are given in table 1.

All parameters for muscular strength are considerably improved at the experimental group after the 10th day unlike control patients where the changes are minimal but with a trend for deterioration especially emphasized after the 6th week from the beginning of treatment. When comparing the girt of the calves, we establish that the patients from the control group have much higher absolute values. At the end of the specialized physical therapy we report an increase in the muscular mass of the calves at the experimental group and a decrease at the control patients as the absolute values get even. In the course of treatment at the experimental group we establish some improvement in the speed of movements, clinically expressed by shortening the time of flexion and extension in the ankle and knee joints, while at the control group patients the time is prolonged.

The results from static balance (Romberg's test and Duncan's test) and gait (by determining cadence and maximum speed for passing 8 meters) are presented in the table 2.

After the applied specialized physical therapy the balance stability gets improved substantially. On the 6th month the patients remain stable for a long time. The specialized physical therapy increases substantially the maximum gait speed and reduces the cadence at the usual speed of movement most vividly expressed on the 6th week of our survey.

The daily application of specialized physical therapy improves the orthostatic reactivity of patients with DN and the orthostatic

Table 2. Changes in static ataxia and gait parameters

Parameters	Group	Beginning (EG=90; CG=34) $\bar{X}\pm S_D$	On the 10 day (EG=90; CG=34) $\bar{X}\pm S_D$	On the 6th week (EG=90; CG=34) $\bar{X}\pm S_D$	On the 6th month (EG=90; CG=34) $\bar{X}\pm S_D$
Romberg's test (s)	EG	15.58±10.35	28.31±16.42***	36.67±18.71***	40.13±19.47***
	CG	19.18±12.70	19.06±12.05	16.82±11.14	14.85±10.61
	p	0.550	**0.002**	**0.001**	**0.001**
Duncan's test (cm)	EG	20.30±7.13	30.50±8.09	32.45±7.12	30.68±7.72
	CG	28.69±10.19	29.94±6.66	28.37±6.90	24.97±7.23
	p	0.067	0.494	**0.001**	**0.001**
Cadence for 8 m of walking (usual gait)	EG	17.40±3.26	16.04±3.02***	15.16±3.11***	15.57±3.69***
	CG	16.35±2.42	16.47±2.53	17.24±1.95***	18.91±2.02***
	p	0.091	0.466	**0.001**	**0.001**
Maximum speed for passing 8 m (cm/s)	EG	107.38±30.93	130.02±32.34***	139.09±26.47***	133.99±28.28***
	CG	104.91±33.89	99.69±25.82	96.65±24.46	85.55±8.53**
	p	0.701	**0.001**	**0.001**	**0.001**

*$\bar{X}$ – average values of studied indicators; S_D – standard deviation; ***p<0.001, **p<0.01 – considerable differences for each group in the course of treatment in comparison with the initial values; p-considerable differences between the experimental group (EG) and the control group(CG). The obtained results were processed statistically using Wilcoxon test (in order to determine the importance of changes Romberg's test and Duncan's test for each group in the course of treatment), the U-criterion of Mann Whitney (in order to be determined the importance of differences between the two groups from Romberg's test and Duncan's test) and Student t-test for the remaining indicators.*

disautoregulation, increases the muscle strength and the muscle mass of the calves, mobilizes the "muscle pump" and improves vein circulation and systemic hemodynamics [22, 31].

Based on the type of the orthostatic reactivity, following the classification of Thulesius (1976), the patients were divided into 3 groups: normotonic orthostatic reactivity (NOR), where the heart rate (HR) increased up to 20 beats per minute (bpm) and the SBP changes were no more than 10 mmHg while standing; a pathological sympathicotonic orthostatic reactivity (SOR), where the HR increased more than 20 bpm and the SBP dropped more than 10 mmHg; and an asympathicotonic orthostatic reactivity (AOR), where no or minimal changes in the HR along with a decrease in the blood pressure were found.

The beneficial effect of the specialized physical therapy on the orthostatic reactivity in DN patients was proved by the change in the percent ratio between the subjects with different types of orthostatic intolerance – a significant increase in the number of the patients with NOR was observed immediately after the end of the PT, reaching 80.3% from the patients with DN after 6 weeks from the treatment onset (Fig. 1).

The effect of the specialized physical therapy on orthostatic autoregulation is probably due to various mechanisms. Yamomoto et al. (1991) have revealed that the physical exercises stimulate the proprioceptive information connected with a static posture and the motor human activity, implemented through the motoric-visceral reflexes. It is well known that the moderate to intensive exercise stimulates the sympathetic nervous system, whereas in the recovery period after physical loading the parasympathetic activity is dominating. Thus, during the orthostasis in healthy

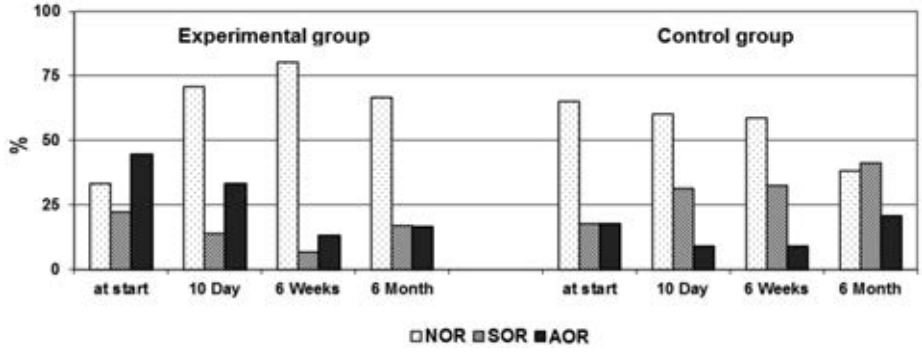

Fig. 1. *Percent distribution of the patients according to the type of the orthostatic reactivity at start, at day 10, 6 weeks and 6 month after the physical therapy onset*

subjects the normal autonomic response provides adaptive changes in the systemic hemodynamics that keep the cerebral circulation stable and prevent from orthostatic hypotension [3, 25].

The patients with DN have a limited motor activity, known to be associated with a decreased physical working capacity, a decreased muscle power, deteriorated nitrogen and protein balance, cardiovascular disturbances and depression [32, 35]. In such patients the appropriate physical exercise can prevent not only the hypokinetic syndrome, but also the development of clinical complications by improving the glucose control and the lipid profile [21] via a normalization of the blood pressure [27], and restoration of the physical and mental health. It has been demonstrated that in patients with DN the exercises, including frequent change on postural body position, stimulate the adaptation of the systemic hemodynamics to orthostatic stimuli mainly through the improvement of the cardiovascular response [1, 13].

Conclusion

Neurorehabilitation is one of the main therapeutic approaches in the whole algorithm of treatment of DN. In compliance with the principal requirements for neurorehabilitation and in particular, physical therapy, the pathogenetic mechanisms and specific symptoms of DN can be positively affected.

The undisputable therapeutic effect of the systemic, continuous specialized physical therapy in patients with DN motivates the necessity of its wider practical application for improving the health status and the health related quality of life of the patients.

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3rd CONGRESS of the Bulgarian Society of Neurosonology and Cerebral Hemodynamics

October 5, 2017 | Sofia, Bulgaria

POSTERS

Poster Session Постерна сесия

NEUROREHABILITATION ***Moderators:*** *D. Lubenova (Bulgaria), D. Vassileva (Macedonia), B. Stamenov (Bulgaria)*		НЕВРОРЕХАБИЛИТАЦИЯ ***Модератори:*** *Д. Любенова (България), Д. Василева (Македония), Б. Стаменов (България)*
Influence of Self-Control Breathing Exercises on Spirometric Parameters in Acute Stroke Patients after Discharge. *K. Grigorova-Petrova, A. Dimitrova, D. Lubenova, M. Nikolova (Bulgaria)*	**P1**	**Влияние на дихателните упражнения върху спирометричните показатели при пациенти с остър инсулт след хоспитализация.** *К. Григорова-Петрова, А. Димитрова, Д. Любенова, М. Николова (България)*
Home-Based Physical Therapy Program in Frontal Ataxia (Case Study). *K. Grigorova-Petrova (Bulgaria)*	**P2**	**Кинезитерапевтична програма при фронтална атаксия в домашни условия (казус).** *К. Григорова-Петрова (България)*
Physiotherapy in Neurological, Respiratory and Metabolic Complications after Cardiac Surgery (Case Study). *I. Alexandrova, Z. Koleva, L. Mitova, K. Grigorova-Petrova, A. Dimitrova (Bulgaria)*	**P3**	**Кинезитерапия при неврологични, дихателни и метаболитни усложнения след кардиохирургична интервенция (казус).** *И. Александрова, Ж. Колева, Л. Митова, К. Григорова- Петрова, А. Димитрова (България)*
Influence of Written Patient Guide for Patients after Lumbar Spine Surgery. *C. Bijeva, D. Lubenova, K. Grigorova-Petrova (Bulgaria)*	**P4**	**Изследване на ефекта от прилагането на писмено ръководство при пациенти след гръбначна операция.** *Ц. Бижева, Д. Любенова, К. Григорова- Петрова (България)*
Influence of Physiotherapy Program Based on the Principles of PNF Concept in Patients with Disc Herniation in Early Postoperative Period. *C. Bijeva, D. Lubenova, K. Grigorova-Petrova (Bulgaria)*	**P5**	**Изследване ефекта от прилагане на PNF методика при пациенти с дискова херния в ранен следоперативен период.** *Ц. Бижева, Д. Любенова , К. Григорова- Петрова (България)*
Practical Application of Graded Repetitive Arm Supplementary Program for Stroke Patients. *Х. Василиу, Д. Захариева, К. Григорова-Петрова (Bulgaria)*	**P6**	**Практическо приложение на допълваща степенувана повтаряща се програма за горен крайник при пациенти с инсулт.** *H. Vasiliu, D. Zaharieva, K. Grigorova-Petrova (България)*
Improving Motor Independence after Supratentorial Unilateral Stroke in the Chronic Period. *D. Vasileva (Macedonia), D. Lubenova (Bulgaria)*	**P7**	**Подобряване на двигателната независимост след супратенториален едностранен мозъчен инсулт в хроничен период.** *Д. Василева (Македония), Д. Любенова (България)*
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Neurorehabilitation in a Case of Myasthenia Gravis. *D. Manov, E. Taseva, S. Toneva, D. Vasileva (Macedonia)*	**P9**	**Неврорехабилитация при миастения гравис.** *Д. Манов, Е. Тасева, С. Тонева, Д. Василева (Македония)*
Effect of Physical Therapy on Static Muscle Endurance in Lumbosacral Pain Syndrome. *M. Nikolova, A. Dimitrova (Bulgaria), D. Vasileva (Macedonia)*	**P10**	**Въздействие на кинезитерапия върху статичната мускулна издържливост при лумбосакрален болков синдром.** *М. Николова, А. Димитрова (България), Д. Василева (Македония)*

Abstracts Резюмета

P1

INFLUENCE OF SELF-CONTROL BREATHING EXERCISES ON SPIROMETRIC PARAMETERS IN ACUTE STROKE PATIENTS AFTER DISCHARGE

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Objective: To establish the ability to influence respiratory functions in acute stroke patients through a feedback breathing device after discharge.

Material and methods: Fifty-nine patients in the acute period after ischemic stroke are monitored. They are divided into two groups, exercise group (EG) and control group (CG), according to their consent of practicing breathing exercises at home. Forced vital capacity (FVC), peak expiratory flow (PEF), forced expiratory volume at 1 s (FEV_1) and inspiratory capacity (IC) are measured in the day of the discharge and one month after the stroke.

Results: There are significant differences in the first month in the PEF and IC between the two groups. All spirometric parameters improve in the EG with significant increase in FEV_1 and IC.

Conclusion: The goal-oriented training by incentive breathing device provides informative feedback on inspiration, facilitates cognitive stage of motor learning by self-control during breathing, and positively influences inspiratory capacity in patients with acute ischemic stroke.

Key words: *acute ischemic stroke, breathing exercises, physiotherapy*

ВЛИЯНИЕ НА ДИХАТЕЛНИТЕ УПРАЖНЕНИЯ ВЪРХУ СПИРОМЕТРИЧНИТЕ ПОКАЗАТЕЛИ ПРИ ПАЦИЕНТИ С ОСТЪР ИНСУЛТ СЛЕД ХОСПИТАЛИЗАЦИЯ

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Цел: Да се определи възможността за повлияване на респираторната функция при инсултно болни в остър период чрез уред за стимулиране на вдишването.

Материал и методи: Проследени са 59 пациента в остър период след исхемичен мозъчен инсулт, разделени в две групи – експериментална и контролна, според желанието им за самостоятелно изпълнение на дихателни упражнения с индивидуален уред. В деня на изписването и един месец след инсулта са проследени: форсиран витален капацитет, върхов експираторен дебит, форсиран експираторен обем за 1 сек и инспираторен капацитет.

Резултати: На първия месец се наблюдават значими разлики между двете групи по отношение на инспираторен капацитет и върхов експираторен дебит. При експерименталната група се отчита подобрение при всички спирометрични показатели, статистически значими при форсирания експираторен обем за 1 sec и инспираторния капацитет.

Заключение: Целенасочената тренировка чрез уред за стимулиране на вдишването осигурява достатъчно информативна обратна връзка, улеснява когнитивния стадий на двигателно обучение чрез самоконтрол върху процеса на вдишване и положително повлиява инспираторния капацитет при пациенти след исхемичен мозъчен инсулт.

Ключови думи: *дихателни упражнения, остър исхемичен мозъчен инсулт, кинезитерапия*

P2

HOME-BASED PHYSICAL THERAPY PROGRAM IN FRONTAL ATAXIA (CASE STUDY)

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Objective: To determine if a home-based physical therapy program was feasible for improving locomotion and balance abilities in frontal ataxia after multi-infarct encephalopathy.

Material and methods: A patient, after four ischemic strokes (the first, 15 years ago), with comorbidity of hypertension and diabetes type II, participated in a four-week individually tailored PT program. Pre- and post-training assessment included neurological examination, Berg Balance Scale (BBS) and Timed Up and Go Test (TUG). The program consisted of 90 min, 3-4 times/week gradually progressive PT sessions with strength training, static and dynamic task practice for trunk and postural control (in sitting and standing) with gradual narrowing the base of support and stress on optimal alignment, sensory training, walking in different environment.

Results: Improvement mostly in anticipatory movement in BBS was observed. The patient improved TUG time with 28 sec, but still had problem with double task.

Conclusion: The targeted home-based physical therapy program improves the functional mobility in case of frontal ataxia. The specific intervention must be designed on every level of function, activities and participation deficits.

Key words: *frontal ataxia, physical therapy*

КИНЕЗИТЕРАПЕВТИЧНА ПРОГРАМА ПРИ ФРОНТАЛНА АТАКСИЯ В ДОМАШНИ УСЛОВИЯ (КАЗУС)

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Цел: Да се определи приложимостта на кинезитерапията в домашни условия за подобряване на равновесните реакции и походката при пациент с мултиинфарктна енцефалопатия.

Материал и методи: Изследването е проведено за 4-седмичен период с пациент, преживял четири исхемични инсулта (първия с 15-годишна давност), със съпътстващи заболявания хипертонична болест и захарен диабет II тип. Преди и след процедурите са извършени следните изследвания: неврологично състояние, Berg Balance Scale (BBS) и Timed Up and Go Test (TUG). Кинезитерапията е с продължителност 90 минути, 3-4 пъти седмично и включва упражнения за мускулна сила, целенасочено трениране на статичен и динамичен постурален контрол (в седеж и стоеж), с постепенно намаляване на опорната площ, с акцент върху оптималното алиниране, сензорна тренировка, ходене в различни условия.

Резултати: Наблюдава се подобрение в BBS, предимно в предварителния контрол. Намалява се времето за TUG, но все още има проблем при изпълнение на TUG с двойна задача.

Заключение: Целенасочената домашна кинезитерапия подобрява функционалната мобилност при пациент с фронтална атаксия като се фокусира на всяко ниво на наличен дефицит.

Ключови думи: *кинезитерапия, фронтална атаксия*

P3

PHYSIOTHERAPY IN NEUROLOGICAL, RESPIRATORY AND METABOLIC COMPLICATIONS AFTER CARDIAC SURGERY (CASE STUDY)

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Objective: To monitor the effect of applied physiotherapy in a patient with complications after aortic valve thrombectomy.

Material and methods: A 73-year-old female 24 days after aortic valve thrombectomy is described. On the 10th day after intervention she presents with ischemic stroke in the right middle cerebral artery (Glasgow-Liege Coma Scale – 20, NIHSS – 5, Chedock MacMaster: arm – stage 4 to stage 5; hand – stage 1 to stage 2; leg – stage 4 to stage 5; foot – stage 3), on the 17th

КИНЕЗИТЕРАПИЯ ПРИ НЕВРОЛОГИЧНИ, ДИХАТЕЛНИ И МЕТАБОЛИТНИ УСЛОЖНЕНИЯ СЛЕД КАРДИОХИРУРГИЧНА ИНТЕРВЕНЦИЯ (КАЗУС)

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Цел: Да се проследи ефекта от прилаганата кинезитерапия при пациент с усложнения след тромбектомия на аортна клапа.

Материал и методи: Проследена е жена на 73 г. три седмици след тромбектомия на аортна клапа. На 10-ия ден след интервенцията получава исхемичен мозъчен инсулт в басейна на дясна средна мозъчна артерия (Glasgow-Лиеж Coma Scale – 20, NIHSS – 5, Chedock MacMaster: горен крайник

day, with hyperglycemic coma, and on the 24th day, with COPD exacerbation. The patient has concomitant diseases: arterial hypertension, congestive heart failure III degree, COPD, type II diabetes mellitus, and diabetic polyneuropathy. Medical condition and vital signs (blood pressure, saturation, heart and respiratory rate), Barthel Index of activities of daily living, Borg Scale for perceived exertion has been monitored. After daily medical condition's assessment the following physical therapy has been applied for two weeks: patient's education about safe bed mobility and activities of daily life, respiratory care, mobilization, specific methods to neurologic deficits and callisthenic exercises.

Results: After the physical therapy, favorable changes in the patient's functional status have been detected. There is an improvement in the patient's independence in performing the daily life activities and increase in oxygen saturation. Dyspnea and fatigue at exercise, as well as the respiratory rate, show a tendency to decrease.

Conclusions: The physical therapy is an integral part of general medical treatment to achieve functional recovery and independence in polymorbide patients.

Key words: *cardiac surgery, physical therapy, polymorbidity, stroke*

– стадий 4 към стадий 5, китка и пръсти – стадий 1 до стадий 2, долен крайник – стадий 4 до стадий 5, стъпало – стадий 3), на 17-ия ден с хипергликемична кома, на 24-ия ден с екзацербация на ХОББ. Съпътстващи заболявания: хипертонична болест, застойна сърдечна недостатъчност ст. III, ХОББ, диабет тип II, диабетна полиневропатия. Ежедневно се проследяват промените в клиничното състояние, основните жизнени показатели (кръвно налягане, кислородна сатурация, сърдечна и дихателна честота), индексът на Бартел за дейностите на ежедневието и скала на Борг за оценка на задух и умора при физическо натоварване. Индивидуални кинезитерапевтични процедури са провеждани в продължение на две седмици, включващи обучение на пациента за безопасно преместване в леглото и дейности от ежедневието, дихателна рехабилитация, специфични кинезитерапевтични методики за неврологичните дефицити и общоразвиващи упражнения.

Резултати: След проведената кинезитерапия, се установиха благоприятни промени във функционалното състояние на пациента. Наблюдава се подобряване на независимостта на болния при извършване на дейностите от ежедневния живот и се повишава кислородната сатурация. Задухът и умората при физическо натоварване, както и дихателната честота показаха тенденция към намаляване.

Заключение: Кинезитерапията е неразделна част от комплексното лечение, за постигане на функционално възстановяване и независимост при полиморбидни пациенти.

Ключови думи: *кардиохирургия, кинезитерапия, мозъчен инсулт, полиморбидност*

P4

INFLUENCE OF WRITTEN PATIENT'S GUIDE FOR PATIENTS AFTER LUMBAR SPINE SURGERY

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Objective: To assess the effect of written patient's guide in patients after lumbar spine surgery.

Material and methods: Forty patients voluntarily attended and treated in the Department of Neurosurgery of the University Hospital Sofiamed, Sofia were randomly divided into two groups (CG n=20) and (EG n=20). The assessment was made on the day of the discharge and one month after surgery. Outcome measures included the Oswestry disability index (ODI) and the Visual analog scale for pain (VAS). The CG was on the standard physical therapy program. A written patient's guide with exercises was given to the patients of EG.

Results: There was an improvement in the two groups for ODI and VAS. Significant differences between the two groups for ODI were found.

Conclusion: The study shows that including a

ИЗСЛЕДВАНЕ НА ЕФЕКТА ОТ ПРИЛАГАНЕТО НА ПИСМЕНО РЪКОВОДСТВО ПРИ ПАЦИЕНТИ СЛЕД ГРЪБНАЧНА ОПЕРАЦИЯ

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Цел: Да се оцени ефекта от използването на писмено ръководство при пациенти след операция на гръбначния стълб.

Материал и методи: Изследвани са четиридесет пациента ,дали доброволно участие, лекувани в Клиниката по неврохирургия на Университетската болница Софиямед – София. Пациентите са разделени на две групи (КГ n=20) and (ЕГ n=20). Изследванията са направени в деня на изписването и един месец след операцията. Тествани са Oswestry disability index (ODI) и Визуално аналогова скала за болка (ВАС). Пациентите от контролната група извършваха стандартната програма за рехабилитация. На експерименталната група беше дадено писменно ръководство за изпълнения на упражнения в домашни условия.

written patient's guide leads to a better outcome one month after spinal surgery.

Key words: *patient's guide, spinal surgery*

Резултати: Наблюдава се подобрение в резултатите на ODI и BAC в двете групи. Разлика в междугруповото разпределение се наблюдава в оценката на ODI един месец след операцията.

Заключение: Проведеното проучване показва, че добавянето на писменно ръководство при пациенти след операция на гръбначния стълб.води до по-добри крайни резутати от изследванията.

Ключови думи: *операция на гръбначния стълб, писменно ръководство*

P5

INFLUENCE OF PHYSIOTHERAPY PROGRAM BASED ON THE PRINCIPLES OF PNF CONCEPT IN PATIENTS WITH DISC HERNIATION IN EARLY POSTOPERATIVE PERIOD

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Objective: To evaluate the effect of applied physiotherapy program based on the principles of PNF concept in patients with lumbar disc herniation in early post-operative period.

Material and methods: Twenty patients with disc herniation treated in the Neurosurgery Department of the University Hospital SofiaMed, Sofia were studied. The quality of life was assessed on the day of discharge and one month after surgery, using a 36-point Quality of Life Scale (SF36). All patients performed physiotherapy program based on the principles of ISF concept for one month after surgery. The methodology was goal-oriented at the overall recovery of the patient, improving the structural and functional level, daily activities, social activity, influencing environmental factors and personal factors.

Results: Improvement in physical health, patients' emotional condition, their social activity and pain symptoms is seen after the physiotherapy program.

Conclusion: The study shows that physiotherapy program based on the PNF concept leads to improvements in the structural and functional status of the patients, their ability to perform daily and social activities.

Key words: *disc herniation, PNF concept*

ИЗСЛЕДВАНЕ ЕФЕКТА ОТ ПРИЛАГАНЕ НА PNF МЕТОДИКА ПРИ ПАЦИЕНТИ С ДИСКОВА ХЕРНИЯ В РАНЕН СЛЕДОПЕРАТИВЕН ПЕРИОД

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Цел: Да се приложи кинезитерапевтична програма, базирана на принципите на PNF методиката върху пациенти с лумбална дискова херния в ранен следоперативен период и да се оцени ефекта от нея.

Материал и методи: Изследвани са 20 болни с дискова херния, оперирани в неврохирургичното отделение на УМБАЛ Софиямед – София. Направена е оценка на качеството на живот в деня на изписването и един месец след операцията, посредством 36-точкова скала за качество на живот (SF36). При всички болни е провеждан кинезитепевтичен комплекс в продължение на един месец след операцията. Методиката е насочена към цялостното възстановяване на пациента, повлияване на структурно и функционално ниво, подобряване на дейности от ежедневието, социална активност, повлияване върху факторите на околната среда и лични фактори.

Резултати: След кинезитерапията се наблюдава подобрение във физическото здраве, емоционалното състояние на пациентите, социалната им активност и болковата симптоматика.

Обсъждане: Проучването показва, че прилагането на кинезитерапевтична методика, базирана на концепцията на PNF, води до подобряване на структурното и функционално състояние на изследваните пациенти и възможността им за извършване на дейности и социална реабилитация.

Ключови думи: *дискова херния, PNF методика, качество на живот*

P6

PRACTICAL APPLICATION OF GRADED REPETITIVE ARM SUPPLEMENTARY PROGRAM FOR STROKE PATIENTS

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Objective: Impaired motor activity of the affected upper extremity is common post stroke and it is recommended to practice movements to regain function. The aim of the study is to explore the effect of self-administered homework-based exercises in subacute stroke patients.

Material and methods: Ten patients (7 men, 3 women, mean age 55.3±10.3) with subacute stroke (2.6±2.45 month's poststroke) were evaluated with Fugl-Meyer Motor Assessment (FMA) for upper extremity, Chedoke Arm and Hand Activity Inventory (CAHAI) and Wolf Motor Function Test (WMFT). The Graded Repetitive Arm Supplementary Program was taught and monitored by a therapist but carried out independently by the patient for 14 consistent physical therapy sessions.

Results: Significant improvement in voluntary movement in functional tasks and activities in daily living was observed.

Conclusion: The applied program enables patients to increase the intensity of use of the affected upper limb after stroke to regain its function.

Key words: *exercises, physical therapy, stroke*

ПРАКТИЧЕСКО ПРИЛОЖЕНИЕ НА ДОПЪЛВАЩА СТЕПЕНУВАНА ПОВТАРЯЩА СЕ ПРОГРАМА ЗА ГОРЕН КРАЙНИК ПРИ ПАЦИЕНТИ С ИНСУЛТ

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Цел: Нарушената двигателна активност на засегнатият горен крайник е често срещан симптом след прекаран инсулт и за функционалното му възстановяване се препоръчва лечение рез движение. Изследването бе проведено с цел да се проучи ефекта на Програма от самостоятелно прилагани упражнения в домашна обстановка в подострата фаза на пациенти, преживяли мозъчен инсулт.

Материал и методи: 10 пациенти (7 мъже и 3 жени, средна възраст 55.3±10.3) в подострата фаза на мозъчен инсулт (средно 2.6±2.45 месеца след инсулта) бяха оценени с Fugl-Meyer Motor Assessment (FMA) за горен крайник, Chedoke Arm and Hand Activity Inventory (CAHAI) и Wolf Motor Function Test (WMFT).

Пациентите бяха обучение в допълващата степенувана повтаряща се програма за горен крайник, но изпълняваха самостоятелно упражненията в продължение на 14 последователни процедури под наблюдението на терапевт.

Резултати: Постигна се значително подобрение във волевите движения на функционалните задачи и дейности от ежедневието.

Заключение: Приложената програма дава възможност на пациентите да увеличат интензивността на използване на засегнатия горен крайник след инсулт, за да възвърнат функцията й.

Ключови думи: *инсулт, кинезитерапия, упражнения*

P7

IMPROVING MOTOR INDEPENDENCE AFTER SUPRATENTORIAL UNILATERAL STROKE IN THE CHRONIC PERIOD

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Objective: To evaluate the effect of the specialized kinesitherapy methodology (SKTM) on the motor independence in patients with supratentorial unilateral stroke in the chronic period (SUSChP).

Material and methods: The study was conducted in 67 patients with SUSChP (56 patients included in the experimental group – 32 men and 24 women, with disease duration 7.8±2.0 months, and 11 patients in

ПОДОБРЯВАНЕ НА ДВИГАТЕЛНАТА НЕЗАВИСИМОСТ СЛЕД СУПРАТЕНТОРИАЛЕН ЕДНОСТРАНЕН МОЗЪЧЕН ИНСУЛТ В ХРОНИЧЕН ПЕРИОД

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Цел: Да се оцени ефекта на специализираната кинезитерапевтична методика (СКТМ) върху двигателната независимост при пациенти със супратенториален едностранен мозъчен инсулт в хроничен период (СЕМИХП).

Материал и методи: Изследването е проведено

the control group – 9 men and 2 women, with disease duration 7.3±1.5 months). To evaluate the changes, Functional Independence Measure test – FIM was used. In the patients from the experimental group treatment with a specialized 10-day KT, continued later as an adapted exercise program at home for a period of 1 month was applied. Control patients followed a conventional 10-day KT.

SKTM follows the principles of modern neurorehabilitation and motor learning, as opposed to usual kinesitherapy. It is based on the fundamental principles of modern neurorehabilitation, namely: to be individualized, intensive, specifically-tailored and focused on the individual needs of the patient. The program needs to be realized with the active participation of the patient and his/her family during long-term care so as to ensure care, tailored to the needs of the patient throughout life, to achieve restoration and influence of the late complications of the disease. This specialized kinesitherapeutic methodology conforms to the principles of motor learning. They are: specificity of the task, active participation of the patient, repetition, adaptation of complexity, feedback, and variability "contextual interference".

Results: After the applied SKTM, the highest tendency towards improvement of the motor independence was established in the 1st month, with a level of significance during treatment $p<0.001$.

Conclusion: Compared with the usual kinesitherapeutic methodology, the applied SKTM in the experimental group later continued as an adapted exercise program at home, significantly improved the motor independence of the patients with supratentorial unilateral stroke in the chronic period.

Key words: *chronic period, kinesitherapy, motor independence, stroke*

при 67 пациенти със СЕМИХП (56 болни включени в експериментална група – 32 мъже и 24 жени, с давност на заболяване 7.8±2.0 месеци, и 11 болни в контролна група – 9 мъже и 2 жени, с давност на заболяване 7.3±1.5 месеци). За оценка на промените е използван тест за функционална независимост Functional Independence Measure – FIM. При пациентите от експерименталната група е проведено лечение със специализирана 10-дневна КТ, която по-късно продължава да се изпълнява като адаптирана програма от упражнения в домашни условия за период от 1 месец. Контролните болни изпълняват обичайна 10-дневна КТ. При СКТМ са спазени принципите на съвременната неврорехабилитация и двигателното обучение, за разлика от обичайната кинезитерапия. Тя е базирана на основните принципи на съвременната неврорехабилитация: да бъде индивидуална, интензивна и специфично ориентирана – съобразена и фокусирана върху индивидуалните потребности на болния; да се реализира с активното му участие и това на неговото семейство, при продължително приложение така, че да гарантира грижи, съобразени с нуждите на болния през целия му живот за постигане на възстановяване и повлияване на късните усложнения от болестта. Специализираната кинезитерапевтична методика спазва и принципите за двигателно обучение: специфичност на задачата, активно участие на пациента, повторение, адаптиране на сложността, обратна връзка, вариабилност „контекстуална намеса".

Резултати: След СКТМ най-висока тенденция към подобрение на двигателната независимост се установи на 1-я месец, с ниво на значимост в хода на лечението $p<0.001$.

Заключение: В сравнение с обичайната кинезитерапия, СКТМ продължена по-късно като адаптирана програма от упражнения в домашни условия, подобрява значимо двигателната независимост на пациентите след преживян супратенториален едностранен мозъчен инсулт в хроничен период.

Ключови думи: *двигателна независимост, кинезитерапия, мозъчен инсулт, хроничен период*

P8

NEUROREHABILITATION OF MULTIPLE SCLEROSIS – A CASE REPORT

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Objective: To follow the influence of the applied neurorehabilitation on a patient with chronic progressive form of multiple sclerosis.

Material and methods: The study is conducted on a 42-year-old female patient with a chronic progressive form of multiple sclerosis within one month at home. The medication therapy includes corticosteroids and Interferon. Kinesitherapy is performed 3 times a week, for one hour, with moderate intensiveness of the stress,

НЕВРОРЕХАБИЛИТАЦИЯ ПРИ МНОЖЕСТВЕНА СКЛЕРОЗА – ОПИСАНИЕ НА СЛУЧАЙ

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Факултет за медицински науки, Университет „Гоце Делчев" – Щип, Македония

Цел: Да се проследи влиянието на неврорехабилитацията при пациентка с хронично-прогресивна форма на множествена склероза.

Материал и методика: Проучването е проведено при жена на 42 г. с хронично-прогресивна форма на множествена склероза в рамките на един месец в домашни условия. Медикаментозната терапия включва кортикостероиди и интерферон. Процеду-

more breaks between the exercises, without getting a level of exhaustion. Correct positioning in the bed and in sitting position, passive/active exercises, analytical exercises for upper and lower extremities, breathing exercises, balance and coordination exercises to sitting and standing, massage treatments are applied. The Berg balance scale and tests for transfer (from occipital laying position to left/right laying position, or to standing position) are used to assess the effects of this therapy. The test Five Times Sit -To- Stand (FTSST) for evaluating the abilities of transfer is used. The changes in the motor activity are monitored twice after discharging from hospital in domestic rehabilitation conditions.

Results: An improvement in the patient's speed of reactions and muscle strength, due to the systematic kinesitherapy procedures and the included exercises for strengthen the lower extremity and abdominal muscles is detected with the transfer tests. The result from the FTSST test is significantly improved, thanks to the improved power of the lower extremities, which is a great step towards the patient's self-sufficiency. The correct position of the thorax and the velocity of movement are of crucial importance. This test evaluates the coordination and consecutiveness of the movements between the thorax and the lower extremities. The improvement of this parameter is due to the described means of kinesitherapy.

Conclusion: Neurorehabilitation is an impotrant tool for improvement of the functional performances and the independence of the patient with MS. Drugs and multi-disciplinary kinesitherapy are proven to be an effective combination in decreasing relapses and functional disability, and thus contributing to the improvement of the quality of life.

Key words: *exercises, kinesitherapy, multiple sclerosis, neurorehabilitation*

рите по кинезитерапия се изпълняват 3 пъти седмично с времетраене от един час, умерена интензивност на натоварването, повече почивка между отделните упражнения, без да се достига до умора. Използва се правилно позициониране в леглото и в седеж, пасивно-активни упражнения, аналитични упражнения за горни и долни крайници, дихателни упражнения, упражнения за равновесие и координация от седеж и стоеж, масажни похвати. За проследяване ефекта от проведената терапия използвахме тестове за трансфер (преминаване от тилен лег до лев/десен страничен лег, от тилен лег до стоеж) и тест на равновесите по скалата на Берг (Berg balance scale). Използвахме и тест „Пет пъти сядане и ставане от стол или легло" – Five Times Sit-To-Stand (FTSST), който е удобен за оценка на възможностите за трансфер. Промените в двигателната активност са проследени двукратно след изписване от болница в условия на домашна рехабилитация.

Резултати: При тестовете за трансфер (преминаване от тилен лег до лев/десен страничен лег, от тилен лег до стоеж) се наблюдава подобрение в бързината на реакциите и мускулната сила на пациентката, което се дължи на системно проведените процедури по кинезитерапия и включените упражнения за сила на долни крайници и абдоминална мускулатура. Резултатът от тестът Five Times Sit-To-Stand (FTSST) е значително подобрен, благодарение на подобрената сила на долните крайници, правилното положение на трупа и бързината на движение. С този тест се преоценява координацията и последователността на движенията между трупа и долните крайници.

Заключение: Неврорехабилитацията допринася за подобряване на функционалните възможности и независимостта на болната с МС. Най-съществен ефект се постига с комбинирано комплексно медикаментозно и мултидисциплинарно рехабилитационно лечение, с цел намаляване на клиничните симптоми на заболяването, намаляване на функционалните дефицити и повишаване на способността за самостойно извършване на ежедневните активности, което допринася за подобряване на качеството на живот.

Ключови думи: *множествена склероза, неврорехабилитация, упражнения*

P9

NEUROREHABILITATION IN A CASE OF MYASTHENIA GRAVIS

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Objective: To trace the impact of the applied neurorehabilitation in a case of generalized adult form of myasthenia gravis.

Material and methods: We describe a 30-year-old female patient with generalized adult form of myasthenia gravis (moderate form). Clinical symptoms started with fatigue, worsening during the day and absent in the

НЕВРОРЕХАБИЛИТАЦИЯ ПРИ МИАСТЕНИЯ ГРАВИС

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Цел: Да се проследи влиянието на приложената неврорехабилитация при пациентка с миастения гравис.

Материал и методи: Проучването е проведено при 30-годишна жена с миастения гравис (средно тежка форма). Клиничните сиптоми са започнали с умора, която се появявала през деня, при отсъст-

morning. Ptosis, diplopia, difficulty speaking, chewing and swallowing, nasal speech, and muscle weakness in upper and lower extremities developed later on. Neurorehabilitation is appointed for a 6-week period at home. The complex includes medication therapy with Prostigmin (15 mg per os) and corticosteroids. The kinesitherapy is performed 3 times a week for one hour, with medium intensity, rest between the separate exercises, without reaching tiredness. Breathing exercises, passive/active exercises, analytical exercises for upper and lower extremities, exercises for improvement of muscle strength, balance and coordination in siting and standing exercises and massages are also used. Muscle weakness tests (MMT), measuring the volume of muscles, Bal's score of subjective pain complains, and squats per minute are used to follow the effect of the applied therapy. The changes in patient's motor activities are checked twice at home.

Results: Measuring the muscle volume in centimeters and the muscle weakness by MMT show improvement of muscle volume and strength, due to the systematic kinesitherapy and strength exercises for upper and lower extremities. The score of subjective complains is lower with decreasing the pain, and the results in the test of squats per minute are significantly improved due to the improved strength of the lower extremities.

Conclusion: The efficiency of the directed and structured exercises is proved by the improvement of the functionality, aerobic capacity for exercising and muscle strength. The biggest benefit is reached by combined complex medication therapy and multidisciplinary rehabilitation, in order to lower the clinical symptoms of the disease and the functional deficits, and improvement of the functional performances. When properly directed and dosed, neurorehabilitation can prevent secondary health issues, such as obesity, coronary heart disease and osteoporosis.

Key words: *kinesitherapy, myasthenia gravis, muscle weakness, neurorehabilitation.*

вие в сутрешните часове. По-късно се появили и птоза и диплопии, затруднения в говора, дъвченето и преглъщането, назален говор, мускулна слабост на горни и долни крайници. Неврорехабилитацията е назначена в рамките на шест седмици в домашни условия, на фона на медикаментозна терапия с простигмин (15 mg per os) и кортикостероиди. Кинезитерапията се изпълнява 3 пъти седмично с времетраене от един час, с умерена интензивност на натоварването, с почивка помежду отделните упражнения, без да се достига до умора. Използват се дихателни упражнения, пасивно-активни упражнения, аналитични упражнения за горни и долни крайници, упражнения за подобряване на мускулната сила, упражнения за равновесие и координация от седеж и стоеж, масажни похвати. За проследяване на ефекта от терапията са приложени тестове за мускулна слабост (ММТ), сантиметрия, балова оценка на субективните оплаквания (болка), клякане за 1 минута. Промените в двигателната активност на пациентката са проследени двукратно в условия на домашна рехабилитация.

Резултати: Сантиметрията и тестът за мускулна слабост (ММТ) показват подобряване на мускулния обем и мускулната сила, което се дължи на системно проведените процедури по кинезитерапия и включените упражнения за сила на горни и долни крайници. Установява се намаляване на баловата оценка на субективните оплаквания за болка. Резултатът от теста с клякания за 1 минута е значително подобрен, което се асоциира с подобрената сила на долните крайници.

Заключение: Ефективността на приложената терапия се доказва чрез подобряване на функционалността, аеробния капацитет при упражняване и мускулна сила. Най-отчетлив ефект се постига с комбинирано комплексно медикаментозно и мултидисциплинарно рехабилитационно лечение, с цел намаляване на клиничните симптоми на заболяването, намаляване на функционалните дефицити и подобряване на функционалните възможности. Насочените и правилно дозирани средства на неврорехабилитация могат да предотвратят развитието на вторичните усложнение като: затлъстяването, коронарната сърдечна болест и остеопороза.

Ключови думи: *кинезитерапия, миастения гравис, мускулна слабост, неврорехабилитация*

P10

EFFECT OF PHYSICAL THERAPY ON STATIC MUSCLE ENDURANCE IN LUMBOSACRAL PAIN SYNDROME

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Objective: To evaluate the effect of physical therapy,

ВЪЗДЕЙСТВИЕ НА КИНЕЗИТЕРАПИЯТА ВЪРХУ СТАТИЧНАТА МУСКУЛНА ИЗДЪРЖЛИВОСТ ПРИ ЛУМБОСАКРАЛЕН БОЛКОВ СИНДРОМ

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including exercises to improve lumbar stabilization in patients with chronic lumbosacral pain syndrome.

Material and methods: 10 patients with chronic lumbosacral syndrome divided into experimental and control groups were examined. Both groups received a physical therapy regimen of individual procedures, 5 times a week for a 6-week course. The physical therapy for the experimental group included warm compresses, massage, breathing exercises, lumbar stabilization exercises, Swiss ball exercises, exercise with Thera-Band and stretching. The control group procedures included massage, breathing exercises, analytical and isometric exercises. For the purposes of the study, changes in the static power endurance of the muscles forming the lumbar muscle corset are double-tracked by the static part of the Kraus–Weber test.

Results: Physical therapy, including exercises to increase lumbar stabilization improves significantly the static muscle endurance in the patients of the experimental group. In the control group there is also positive changes, but the values are less pronounced.

Conclusions: The application of physical therapy, including exercises for lumbar stabilization, exercises with Swiss ball and elastic bands, in combination with warm compresses and stretching, leads to improved static power endurance and strengthens the muscle corset in patients with chronic lumbosacral syndrome.

Key words: *chronic lumbosacral syndrome, lumbar stabilization, static power endurance.*

Цел: Да се оцени ефекта на кинезитерапия с включени упражнения за подобряване на лумбалната стабилизация при пациенти с хроничен лумбосакрален болков синдром.

Материал и методи: Изследвани са 10 болни с хроничен лумбосакрален синдром разделени на експериментална и контролна група. И на двете групи е приложен кинезитерапевтичен курс с индивидуални процедури, 5 пъти седмично в рамките на 6 седмици. При експерименталната група методиката на кинезитерапията се състои от топли компреси, масаж, дихателни упражнения, упражнения за лумбална стабилизация, упражнения на Швейцарска топка, упражнения с Тера-Банд ленти и страчинг. На контролната група са включени масаж, дихателни упражнения, аналитични и изометрични упражнения. За целите на проучването двукратно са проследени промените в статичната силова издържливост на мускулите формиращи поясния мускулен корсет чрез статичната част от теста на Краус–Вебер.

Резултати: Кинезитерапия с включени упражнения за подобряване на лумбалната стабилизация подобрява значимо статичната мускулна издържливост при пациентите от експерименталната група. В контролната група също са налице положителни промени, но стойностите са по-слабо изразени.

Изводи: Прилагането на кинезитерапия с включени упражнения за лумбална стабилизация, упражнения с Швейцарска топка и еластични ленти, в комбинация с апликация на топли компреси и стречинг води до подобряване на статичната силова издържливост и засилване на мускулния корсет при болни с хроничен лумбосакрален синдром.

Ключови думи: *статично силова издържливост, хроничен лумбосакрален синдром, лумбална стабилизация.*

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