

Five Padua days on muscle and mobility medicine (2024Pdm3) 27 February - 2 March, 2024 at Hotel Petrarca, Thermae of Euganean Hills, Padua, and San Luca Hall, Prato della Valle, Padua, Italy

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Abstract

At the end of the 2023 Padua Days of Muscle and Mobility Medicine the next year's meeting was scheduled from 27 February to 2 March 2024 (2024Pdm3). During the summer and autumn the program was confirmed with Scientific Sessions that will take place over five days, starting in the afternoon of February 27, 2024 at the Conference Room of the Hotel Petrarca, Thermae of Euganean Hills (Padua), Italy. As usual, the next day will be spent in Padua, in this occasion at the *San Luca Hall* of the Santa Giustina monastery in Prato della Valle, Padua, Italy. Collected during Autumn 2023, many more titles and abstracts than expected were submitted, forcing the organization of parallel sessions both on March 1 and March 2 2024 confirming attractiveness of the 2024 Pdm3. The five days will include oral presentations of scientists and clinicians from *Argentina, Austria, Belgium, Brazil, Canada, Denmark, Egypt, France, Germany, Iceland, Ireland, Italy, Romania, Russia, Slovenia, Switzerland, UK and USA*. Together with the preliminary Program at December 1, 2023, the early submitted Abstracts is e-published in this Issue 33 (4) 2023 of the European Journal of Translational Myology (EJTM). You are invited to join, submitting your Last Minute Abstracts to ugo.carraro@unipd.it by February 1, 2024. Furthermore, with the more generous deadline of May 20, 2024, submit please "Communications" to the European Journal of Translational Myology (Clarivate's ESCI Impact factor 2.2; SCOPUS Cite Score: 3.2). See you soon at the Hotel Petrarca in Montegrotto Terme, Padua, on February 27, 2024, but the complete program can be followed from home via zoom connection.

Key Words: Padua Days of Muscle and Mobility Medicine; Pdm3 preliminary program; European Journal of Translational Myology, PAGEpress; Italy.

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The meetings on biology, physiology and rehabilitation of skeletal muscle, called Padua Muscle Days (PMDs),

started more than 30 years ago, specifically to provide advice on Translational Myology and Mobility Medicine. Always the interest was on implementing basic research

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and clinical trials to prevent, manage and rehabilitate young adults and elderly persons suffering with mobility disorders. As the final event of the 2023 Padua Days of Muscle and Mobility Medicine (Pdm3, the new nickname of the series) the 2024 meeting was planned to be held from February 27 to March 2, 2023. The success of the registrations and the maintenance of the traditional plan of oral presentations only (in person - the vast majority - or via Zoom), i.e. without poster presentations, forced the organizers to extend the program to five days and to add parallel sessions the March 1st and 2nd, 2024.

The Scientific Program will start on the afternoon of February 27, 2024 with a long Session I dedicated to Electrical Stimulation in Muscle Disorders (Ines Bersch and Winfried Mayr, Chairs) in the Conference Hall Paradise of the Hotel Petrarca, Thermae of Euganean Hills (Padua), Italy. After opening greetings from the Rectorate of the University of Padova, Padua, Italy, the Lecture of Charlotte Suetta, University of Copenhagen, Denmark: Effects of bed rest and immobilisation in young and old individuals – NMES as a potential countermeasure will open the scientific session. A long afternoon will be closed with the Practical Activities I: DM-FES and NMES of Muscles (Ines Bersch, Helmut Kern, Chairs), the Conclusive remarks of Winfried Mayr, Medical University of Vienna, Center for Medical Physics and Biomedical Engineering, Vienna, Austria and at 07:30 PM with a glass of Prosecco before dinner. As usual, the second day of the 2024Pdm3 will be spent in Padua: In this occasion at the *San Luca Hall* of the *Monastero di Santa Giustina* near *Prato della Valle*, Padua, Italy. It is worth to mention that San Luca is the patron of medical activities and we will be near to the first major church of Padua dedicated to Santa Giustina, just sud-west of the Prato della Valle, the biggest square in Europe and possibly of the world. Thus it will be an exciting day with Session II on “Sarcomeric Muscles: regeneration and managements” (Piera Smeriglio, Massimo Ganassi, Chairs) in the morning and in the afternoon Session III-a “Senescence and Rejuvenation of Sarcomeric Muscles” (Kate Kosmac, Christiaan Leeuwenburgh, Chairs) and Session III-b: Rejuvenation of Sarcomeric Muscles: Molecular approaches (Sestina Falcone, Russel Hepple, Chairs). The Lecture of H. Lee Sweeney, University of Florida, FL, USA: Progress toward designing a micro-dystrophin to rescue all striated muscles will open the scientific sessions, while the Lecture of Gillian Butler-Browne, Center of Research in Myology, Sorbonne Universités, Paris, France: Oculopharyngeal Muscular Dystrophy (OPMD) and muscle ageing, it will close an exciting day. February 29, 2024 will be dedicated in the Conference Hall Paradise, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy to Session IV-a dedicated to the impact on human physiological systems of inactivity (Marco Narici, Rado Pisot, Gianni Biolo, Chairs); Session IVb to responses to retraining following bed-rest (Marco Narici, Bostjan Simunič, Chairs) and session V to the impact of activity



Fig 1. Sponsors and Patrons of the 2024Pdm3, February 27 – March 2
Thermae of Euganean Hills and Padua, Italy.

on human behaviors (Daniela Taviani, Roger Coletti, Chairs). The lecture of Roger Coletti Interventional Health, PA, USA: Etiology, identification and treatment of chronic muscle spasm and resultant chronic pain with the CMECD® procedure will open the session VI of February 29, 2024 dedicated to Myo Pain (James R. Friction, Lucrezia Tognolo, Chairs).

Friday March 1 and 2 the program will be split in two parallel sessions to be held either in the Conference Hall Paradise, or in the Conference Room Grazia of the Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy.

In the latter thanks to the initiative of a young dentistry surgeon, Riccardo Rosati of the Milan University (Italy) the March 1, 2024 international Speakers will fill the Program of Session VIIb: Muscle Rehabilitation in Dentistry, while the day after (Saturday March 2, 2024) a Masterclass chaired by Claudia Dellavia and Riccardo Rosati on “Masticatory muscles function maintenance and restoration in daily dentistry” will be dedicated with a practical approach to discussion with Italian

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practitioner. Meantime in the Conference Hall Paradise, of the Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy, Friday March 1, 2024 the Session VII: Hyaluronans and glycosylated proteins in mobility disorders (Elena Barbieri, Carla Stecco, Chairs) will be open at 9: AM by the Lecture of Capucine Trollet, Sorbonne Université, Paris, France: Cellular actors and ECM components of human fibrosis in myopathies.

In the afternoon, the Session VIII: Functional studies from muscle fibers to muscle in situ (Simona Boncompagni, Carlo Reggiani, Chairs) will be open by the Lecture of Feliciano Protasi, University of Chieti, Italy: Remodeling of intracellular organelles during exercise: muscle strategies to reduce muscle fatigue. After a coffee break, it will follow the Session IX: Muscle imaging and digital health in Mobility Medicine (Paolo Gargiulo, Ugo Carraro, Chairs). The Lectures of Paolo Gargiulo, University of Reykyavik, Iceland: Advancing assessment and diagnostic with the use of virtual histology and 3D techniques and the Lecture of Simona Boncompagni, University of Chieti, Italy: Calcium Entry Units (CEUs): dynamic intracellular junctions in skeletal muscle fiber will open and close Session IX.

Saturday March 2, 2024 the morning Session X: LBI workshop on muscle rehabilitation (Sandra Zampieri, Feliciano Protasi, Chairs) will offer a fresh representation of the actual research activities of traditional players of the Padua Muscle days: The Vienna Group founded and still lead by Helmut Kern with the help of ex-young and very young collaborators.

Finally, in the afternoon Practical Activities III: Underwater physiotherapy and Home Full-Body in Bed-Gym, (Helmut Kern, Maria Chiara Maccarone, Chairs) and the Session XI: World Federation of Hydrotherapy (FEMTEC) (Elena P. Ivanova, Stefano Masiero, Chairs) will present a program inspired to our 2024Pdm3 Conference Site: The 3000-year-long tradition of warm waters and mud treatments of neuromuscular and osteoarticular disorders and pain in the Thermae of Euganean Hill, Padua, Italy. In conclusion, the five days include oral presentations of senior and junior scientists and clinicians from *Argentina, Austria, Belgium, Brazil, Canada, Denmark, Egypt, France, Germany, Iceland, Ireland, Italy, Romania, Russia, Slovenia, Switzerland, UK, and USA.*

Together with the preliminary Program at November 25, 2023, a Collection of Early Submitted Abstracts is e-published in this Issue 33 (4) 2023 of the European Journal of Translational Myology (EJTM). In the following Collection there are some empty Abstracts (only names and affiliations of authors). A few of them are just unsubmitted abstracts from high-level speakers invited by long-term PMD Feriends who don't bother publishing conference abstracts, but meanwhile underestimate their value to educate young readers. Most have been decisions by speakers to do not publish in this Issue their original results deserving full articles in prestigious journals. We found the latter a strong

evidence of relevance of 2024Pdm3 that is attracting speakers and presentations with original results from top labs studying muscle and mobility medicine. We apologize to the readers for having decided to keep those speakers in the Program of the 2024Pdm3.

In any case we are sure that 2024Pdm3 will be even more successful than the successful events of the last years.¹⁻⁸

List of acronyms

EJTM - European Journal of Translational Myology
Pdm3 - Padua Days on Muscle and Mobility Medicine
PMD – Padua Muscle Days

Acknowledgments

The authors thank Organizers, Chairs, Lecturers, Speakers and Attendees for their scientific and personal financial contributions to the organization and success of the 2024Pdm3. The previous Figure 1 depicted our many Patrons and (few) Sponsors, but we must highlight the two most generous, i.e., H. Lee Sweeney, Director of the Myology Institute at the University of Florida, Gainesville, FL, USA, whose generous donation allowed all lecturers and speakers who had to cover costs of



transatlantic travel to be exempt from registration fees.

Furthermore, the Gastaldello Family of Hotel Petrarca, Montegrotto Terme, Padua, Italy for a generous donation



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Conflict of Interest

The authors disclose no conflicts of research interest.

Ethical Publication Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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Preliminary program of the 2024Pdm3

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2024 Padua 5 Days on Muscle and Mobility Medicine (2024Pdm3)

February 27,28,29 and March 1,2, 2024 - *Thermae of Euganean Hills, Padua (Italy)*

Hotel Petrarca, Piazza Roma 23, Montegrotto Terme, Euganean Hills, (Padua), 35122 Italy

Phone +39 049 891 1744 - Email: petrarca@hotelpetrarca.it - <https://www.hotelpetrarca.it/>



Organizers: Elena Barbieri, Ines Bersch-Porada, Ugo Carraro, Raffaele De Caro, James R. Friction, Massimo Ganassi, Paolo Gargiulo, Elena P. Ivanova, Helmut Kern, Christiaan Leeuwenburgh, Alessandro Martini, Stefano Masiero, Marco V. Narici, Philippe Perrin, Riccardo Rosati, Marco Sandri, Piera Smeriglio, Carla Stecco, H. Lee Sweeney, Daniela Tavian, Sandra Zampieri

TUESDAY February 27, 2024

Conference Hall Paradise, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

- 03:00 PM Openings: Antonio Paoli, Greetings from the Rectorate of the University of Padua
- 03:10 PM **SESSION I: FES management of diseased muscle**, Ines Bersch, Winfried Mayr, Chairs
- 03:10 PM Stefano Schiaffino: Introductory words for Charlotte Suetta's Lecture
- 03:20 PM Lecture of Charlotte Suetta, University of Copenhagen, DK: Effects of bed rest and immobilisation in young and old individuals – NMES as a potential countermeasure
- 04:00 PM Muscular dystrophies – case series from a clinical point of view with FES, Ines Bersch-Porada, Marie Alberty, International FES Centre®, Swiss Paraplegic Centre Nottwil, Switzerland
- 04:20 PM Surface Electrostimulation stops Denervated Muscle Atrophy in Facial Paralysis, Johannes Krauss, Gert Volk, Department of Otorhinolaryngology, Jena University Hospital, Germany
- 04:40 PM NMES in skin disorders, Giovanna Albertin, Human Anatomy, DNS, University of Padua, Italy
- 05:00 PM Paired stimulation for denervated muscle in persons with SCI: A Proposed Study, Ashraf Gorgey, School of Medicine, Virginia Commonwealth University, Richmond, VA, USA
- 05:20 PM Perspectives of over 20 years of FES to treat equine muscle spasms and the potential crossover into humans, Sheila Schils, EquiNew, River Falls, Wisconsin, USA
- 05:40 PM Towards patient-controlled skeletal muscle pacemaker for SCIs, Mohamed Abbas, Faculty of Engineering, Assiut University, Egypt
- 06:00 PM Practical Activities I: DM-FES and NMES of muscles, Ines Bersch, Helmut Kern, Chairs
- 06:00 PM Electric stimulation for Bell's palsy, Myriam Loyo, Michelle Cameron, Department of Otolaryngology – Head and Neck Surgery, Oregon Health Science University, Portland, OR, USA & Antonio Di Pietro, Department of Biophysics, Universidad of Córdoba, Argentina
- 06:30 PM FES for Denervated Degenerating Muscles (DDM): ten years of experience, Helmut Kern, Ludwig Boltzmann Institute for Rehabilitation Research, Vienna, Austria & Ugo Carraro, Department of Biomedical Sciences, University of Padua, Italy
- 07:00 PM Conclusive remarks, Winfried Mayr, Medical University of Vienna, Center for Medical Physics and Biomedical Engineering, Vienna, Austria
- 07:30 PM *A glass of Prosecco before dinner*

WEDNESDAY February 28, 2024

San Luca Hall, Santa Giustina Monastery, Prato della Valle, Padua, Italy

REACHABLE FROM VIA GIUSEPPE FERRARI 2, 35123 - Padua, Italy

- 08:00 AM** **Complimentary Bus from Hotel Petrarca to Prato della Valle, Padua, Italy**
- 08:40 AM** **SESSION II: Sarcomeric Muscles: development, regeneration and managements,**
Piera Smeriglio, Massimo Ganassi, Chairs
- 08:40 AM** **Lecture of H. Lee Sweeney, University of Florida, Gainesville, FL, USA**
Progress toward designing a micro-dystrophin to rescue all striated muscles
- 09:20 AM** **Skeletal muscle response after treatment in spinal muscular atrophy, Piera Smeriglio, Sorbonne Université, Centre de Recherche en Myologie UMRS 974, Institut de Myologie, Paris, France**
- 09:40 AM** **Satellite Cell-opathies and where to find them, Massimo Ganassi, King's College London, UK**
- 10:00 AM** **Cancer cachexia and precision medicine, Marco Sandri, DBS, University of Padua, Italy**
- 10:20 AM** **Mitochondria network dynamics in human cancer cachexia, Sandra Zampieri, DISCOG, University of Padua, Italy**
- 10:40 AM** **Open Coffee**
- 10:50** **Neuromuscular coordination: from birth to adulthood, Francesco Lacquaniti, University of Rome II, Italy**
- 11:10 AM** **Advancing assessment and diagnostic with the use of virtual histology and 3D techniques, Paolo Gargiulo, University of Reykyavik, Iceland**
- 11:30 AM** **Motor unit alteration following MBNL functional loss in myotonic dystrophy, Denis Furling, Sorbonne Université, Centre de Recherche en Myologie UMRS 974, Institut de Myologie, Paris, France**
- 11:50 AM** **Unraveling the Effects of Time Restricted Eating on Inflammation and Related Biological Processes, Steve Anton, Dept. of Physiology and Aging, College of Medicine, and Dept of Clinical and Health Psychology, University of Florida, Gainesville, USA**
- 12:10 AM** **IGF-I from fibroadipogenic progenitors is a critical modulator of muscle regeneration, Elisabeth Barton, University of Florida, FL, USA**
- 12:30 AM** **Lunch: "Veganda", via Cavazzana 1, Prato della Valle, Padua, Italy**
- 02:00 PM** **SESSION III-a: Senescence & Rejuvenation of Sarcomeric Muscles,**
Kate Kosmac, Christiaan Leeuwenburgh, Chairs
- 02:00 PM** **Immunomodulation of skeletal muscle regeneration: muscle macrophages and beyond, Kate Kosmac, Department of Physical Therapy, College of Allied Health Sciences, Augusta University, Augusta, Georgia, USA**
- 02:20 PM** **Updates on Clinical Trials Boosting NAD+ levels by Supplementation of NR or NMN to promote Rejuvenation, Christiaan Leeuwenburgh, University of Florida, Gainesville, FL, USA**
- 02:40 PM** **Mediators of youthfulness in skeletal muscle, Kevin Murach, Department of Health, Human Performance and Recreation, University of Arkansas, Fayetteville, AR, USA**
- 03:00 PM** **GDF5-based therapeutic approach to counteract age-related muscle wasting, Sestina Falcone, Sorbonne Université, Paris, France**
- 03:20 PM** **Proteomic profiling of fibre type shifting in aged skeletal muscles, Kay Ohlendieck, Department of Biology, Maynooth University, Maynooth, Co. Kildare, Ireland**
- 03:40 PM** **Circadian Catecholamine Sensitivity: Does Time Matter? Ken Dyar, Institute for Diabetes and Cancer, Helmholtz Munich, Germany**
- 04:00 PM** **Coffee break**

WEDNESDAY February 28, 2024

San Luca Hall, Santa Giustina Basilica, Prato della Valle, Padua, Italy

REACHABLE FROM VIA GIUSEPPE FERRARI 2, 35123 - Padua, Italy

04.20 PM SESSION III-b: Rejuvenation of Sarcomeric Muscles: Molecular approaches,

Sestina Falcone, Russel Hepple, Chairs

04:20 PM Contractile activity and mitochondrial transplantation rescue lysosomal and mitochondrial homeostasis in muscle cells, David Hood, York University, Canada, Canada

04:40 PM Role of mitochondrial permeability transition in driving skeletal muscle pathology in aging and disease, Russel Hepple, University of Florida, Gainesville, FL, USA

05:00 PM Exercise rescues the negative effects of head-down tilt bed rest on muscle and mitochondrial health in older adults, Gilles Gousspillou, Faculty of Sciences, Université du Québec at Montréal, Quebec, Canada

05:20 PM Mitochondrial stress response in muscular dystrophy and cancer cachexia, Christopher Perry, School of Kinesiology & Health Sciences, York University, ON, Canada,

05:40 PM The role of the Mitochondrial Calcium Uniporter in skeletal muscle in health and disease, Agnese De Mario, DBS, University of Padua, Italy,

06:00 PM The energetic expense of inflammation: implications for muscle health, -Springer, Department of Animal Science, Department of Kinesiology & Sport Management Texas A&M University, College Station, Texas, USA

06:20 PM Lecture of Gillian Butler-Browne, Center of Research in Myology, Sorbonne Universités, Paris, France

Oculopharyngeal Muscular Dystrophy (OPMD) and muscle ageing

07:00 PM *Complimentary Bus from Prato della Valle, Padua to Hotel Petrarca, Montegrotto Terme (Padua,) Italy*

07:30 *Dinner in Hotel Petrarca*

THURSDAY FEBRUARY 29, 2024

Conference Hall Paradise, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

08:30 AM **SESSION IV-a: Impact of inactivity on human physiological systems,**

Marco Narici, Rado Pisot, Gianni Biolo, Chairs

- 08:30 AM Simulating weightlessness with inactivity models on Earth: research experience of the Bedrest Centre in Koper, Rado Pišot, et al., Institute for Kinesiology Research, Science and Research Centre Koper, Slovenia
- 08:50 AM Neuromuscular impairment with chronic inactivity, Marco Narici, et al., Department of Biomedical Sciences, University of Padova, Padua, Italy
- 09:10 AM Mononuclear resident cells and skeletal muscle homeostasis in disuse: an overview, Roberto Bottinelli, et al., Department of Molecular Medicine University of Pavia, Italy
- 09:30 AM Skeletal muscle oxidative metabolism following disuse/microgravity: where are the bottlenecks? Bruno Grassi, Giovanni Baldassarre, Lucrezia Zuccarelli, Department of Medicine, University of Udine, Udine, Italy
- 09:50 AM Muscle sparing effect of high-protein diet with excess leucine in short-term bed rest, Gianni Biolo, et al., Department of Medical Surgical and Health Science, University of Trieste, Italy
- 10:10 AM *Open Coffee*
- 10:20 AM Physical inactivity and mitochondria. Challenging the paradigm, Marta Murgia, et al., DBS, University of Padua, Italy and Max-Planck-Institute of Biochemistry, Martinsried, Germany
- 10:40 AM Sensitivity of mitochondrial respiration to submaximal [ADP] after bed rest: a new approach based upon different mitochondrial populations, Lucrezia Zuccarelli, et al., Department of Medicine, University of Udine, Udine, Italy
- 11:00 AM Mitochondrial and Neuromuscular Junction Alterations with Chronic Inactivity in Humans, Evgeniia Motanova, et al., Department of Biomedical Sciences, University of Padova, Padua, Italy
- 11:20 AM Motor unit properties alterations with chronic inactivity in young and older humans, Fabio Sarto, et al., Department of Biomedical Sciences, University of Padova, Padua, Italy
- 11:40 AM Sensorimotor adaptations during bed rest: insights from high-density electroencephalography, Uros Marusic, et al., Institute for Kinesiology Research, Science and Research Centre Koper, Koper, Slovenia
- 11:50 AM Effect of prolonged bed rest on brain functional connectivity measured with high-density electroencephalography, Marco Marino, et al., Department of General Psychology, University of Padova, Padua, Italy
- 12:00 AM The relevance of Tensiomyographic results in disuse studies, Bostjan Simunič, et al., Institute for Kinesiology Research, Science and Research Centre Koper, Koper, Slovenia
- 12:20 PM **SESSION IV-b: Impact of inactivity on human physiological systems: Physiological responses to retraining following inactivity.** *Bostjan Simunič, Marco Narici, Chairs*
- 11:20 PM Previous muscle disuse influences the physiological adaptations to exercise recovery, *Martino Franchi*, et al., Human Neuromuscular Laboratory, Department of Biomedical Sciences, University of Padua, Italy
- 12:40 AM Effects of disuse and retraining on oxygen diffusion and oxidative capacity at skeletal muscle level, Simone Porcelli, et al., Department of Molecular Medicine University of Pavia, Italy
- 01:00 PM Neuromodulatory contribution to lower limb muscle force production after short-term unloading and active recovery, Giovanni Martino, et al., Department of Biomedical Sciences, University of Padova, Padua, Italy
- 01:20 PM *Lunch*

THURSDAY FEBRUARY 29, 2024

Conference Hall Paradise, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

- 02:30 PM** **SESSION V: Impact of activity on human behaviors**, Daniela Tavian, Roger Coletti, Chairs
- 02:30 PM** Ketogenic diet, health and exercise, Antonio Paoli, University of Padova, Padua, Italy
- 03:00 PM** Optimizing home Full-Body in Bed-Gym, Maria Chiara Maccarone, University of Padova, Padua, Italy
- 03:20 PM** Cardiorespiratory and neuromuscular adaptations induced by strength training and low-volume, high-intensity aerobic training in untrained young people, Paulo Gentil, College of Physical Education and Dance, Federal University of Goias, Goiania, Brazil
- 03:35 PM** Effects of high intensity vs. continuous interval training on cardiac autonomic modulation of hypertensive women, Paulo Gentil, College of Physical Education and Dance, Federal University of Goias, Goiania, Brazil
- 03:50 PM** β -endorphin induction following acute physical exercise in young and middle-aged adults, Ester Tommasini, et al., UCSC, Milan, Italy
- 04:00 PM** Brain-Derived Neurotrophic Factor production in response to strenuous incremental exercise across adulthood, Luigi Marano, et al., UCSC, Milan, Italy
- 04:10 PM** The impact of the isocapnic hyperpnea respiratory muscle training on diaphragm structure and function, Marta Borrelli, et al., University of Milan, Milan, Italy
- 04:20 PM** *Open Coffee*
- 04:20 PM** **SESSION VI: Myo Pain**, James R. Friction, Lucrezia Tognolo, Chairs
- 04:20 PM** Lecture of Roger Coletti, Interventional Health, PA, USA: Etiology, identification and treatment of chronic muscle spasm and resultant chronic pain with the CMECD® procedure
- 05:00 PM** Predicting development of musculoskeletal pain, Lars Arendt-Nielsen, Aalborg University Hospital, Aalborg, Denmark
- 05:30 PM** Transformative care for myopain: Integrating training with treatment to improve long-Term outcomes, James Friction, Minnesota Head and Neck Pain Clinic, Professor Emeritus, University of Minnesota, USA
- 06:00 PM** The role of external-focus exercise & exergaming in pain management, Jan Dommerholt, Department of Physical Therapy and Rehabilitation Science, School of Medicine, University of Maryland, Baltimore, Maryland, USA
- 06:20 PM** Anti-pain rehabilitation management of muscle injuries, Lucrezia Tognolo, et al. Rehabilitation Unit of DNS, University of Padua & General Hospital, Padua, Italy
- 06:40 PM** New frontiers in the treatment of pain in acute plantar fasciitis: Ozoile-soaked taping, Giuseppe Secolo et al., Faculty of Medicine and Pharmacy, University Dunarea de Jos, Galati, Romania
- 07:00 PM** Perspectives of over 20 years of FES to treat equine muscle spasms and the potential crossover into humans, Sheila Schils, EquiNew, River Falls, Wisconsin, USA
- 07:30 PM** *Dinner*

2024Pdm3 February 27 to March 2, 2024 – Program and abstracts of five Padua Muscle Days

Eur J Transl Myol 33 (04) 12161. doi: 10.4081/ejtm.2023.12161

FRIDAY March 1, 2024

Conference Hall Paradise, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

- 09:00 AM** **SESSION VII: Hyaluronans and glycosylated proteins in mobility disorders,**
Elena Barbieri, Carla Stecco, Chairs
- 09:00 AM** Lecture of Capucine Trollet, Sorbonne Université, Paris, France: Cellular actors and ECM components of human fibrosis in myopathies
- 09:40 AM** Hyaluronan and aging, *Carla Stecco, DNS, University of Padua, Italy*
- 10:00 AM** How denervation influences the fascia, HA Xiaoxiao Zhao, DNS, University of Padua, Italy
- 10:20 AM** Ultrasound evaluation of the fascial gliding, Carmelo Pirri, DNS, University of Padua, Italy
- 10:40 AM** *Coffee break*
- 11:00 AM** Hyaluronans and glycosylated proteins in mobility disorders: from research to clinical applications, Elena Barbieri and Giosuè Annibalini, University of Urbino Carlo Bo, Italy
- 11:40 AM** Hyaluronic acid-extracellular vesicles interactions: pathological and therapeutic implications in osteoarthritis, Piero Sestili, University of Urbino Carlo Bo, Italy
- 12:00 AM** Calcium crystal and glycosaminoglycan in the synovial fluid of patients with femoroacetabular impingement: impact on joint mobility, Michela Battistelli, University of Urbino Carlo Bo, Italy
- 12:30 AM** *Lunch*
- 02:00 PM** **SESSION VIII: Functional studies from muscle fibers to muscle in situ**
Simona Boncompagni, Carlo Reggiani, Chairs
- 02:00 PM** Lecture of Feliciano Protasi, University of Chieti, Italy: Remodeling of intracellular organelles during exercise: muscle strategies to reduce muscle fatigue,
- 02:40 PM** The ERG1A K⁺ Channel Lowers Expression of Calsequestrin 1 and Increases Intracellular Calcium in Skeletal Muscle, Amber Pond, Anatomy Department, Southern Illinois University, School of Medicine, Carbondale, Illinois, USA
- 03:00 PM** Cytosolic Ca²⁺ gradients and mitochondrial Ca²⁺ uptake in resting muscle fibers: A model analysis, Lorenzo Marcucci, Carlo Reggiani, DSB, University of Padua, Italy
- 03:20 PM** Comparison of dysferlin expression in different muscles, Marija Meznaric, Corrado Angelini, Faculty of Medicine, University of Ljubljana, Slovenia
- 03:40 PM** The role of Akt-mTORC1 signaling in regulating muscle mass and function, Bert Blaauw, et al., DSB, University of Padua, Italy
- 04:00 PM** *Coffee Break*
- 04.20 PM** **Session IX: Muscle imaging and digital health in Mobility Medicine**
Paolo Gargiulo, Ugo Carraro, Chairs
- 04:20 PM** Lecture of Paolo Gargiulo and Riccardo Forni, University of Reykjavik, Iceland
New direction of medical imaging transformation
- 05:00 PM** Redlan: an alternative method for analyzing electromyographic data in orthodontics. Lanfranco Vespertini, Bstat, DSc (Econ), Verona, Italy
- 05:20 PM** Dynamic Ecomyography and 3D Muscle Color CT for aging countermeasures: An educational case report, Daniele Coraci, et al., DNS, University of Padua, Italy
- 05:40 PM** Neurophysiology and advanced imaging to investigate muscular morphology and function in adolescent idiopathic scoliosis, Maria Chiare Maccarone et al., DNS, University of Padua, Italy
- 06:00 PM** Foot drop syndrome: neurophysiological and ultrasound approach in the evaluation of SPE deficit, Emanuele D'Andria, et al., Rehabilitation Unit of DNS, University of Padova, Padua, Italy
- 06:20 PM** Impact of low muscle mass and myosteatosis on the surgical outcome of patients with esophagogastric cancer, Elisa Sefora Pierobon, et al., DiSCOG, University of Padua, Italy
- 06:40** Lecture of Simona Boncompagni, University of Chieti, Italy: Calcium Entry Units (CEUs): dynamic intracellular junctions in skeletal muscle fibers
- 07:30 PM** *Dinner*

FRIDAY MARCH 1, 2024

Conference Hall Grazia, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

- 09:00 AM** Welcome and thanks, Riccardo Rosati, Milan, Italy
- 09:10 AM** **SESSION VII-b: Muscle Rehabilitation in Dentistry**, *Elena P. Ivanova, Riccardo Rosati, Chairs*
- 09:10 AM** How to diagnose temporomandibular disorders and the 10 key points in the temporomandibular practice, Matteo Val, University of Siena, Italy
- 09:40 AM** The management of TMD based on multimodal therapy: the state of the art. Roberto Rongo, University of Naples Federico II, Italy
- 10:00 AM** How and when joint surgical therapy is necessary, Luca Guarda-Nardini, University of Padua, Italy
- 10:20 AM** How and when instrumental diagnostics of the masticatory muscles can tell us something more. Claudia Dellavia, University of Milan, Italy
- 10:40 AM** Coffee break
- 11:00 AM** Muscle evaluation as an orthodontic prognosis tool. Redento Peretta. Vicenza, Italy
- 11:20 AM** Adaptation of the masticatory muscles to orthodontic treatment with aligners, Giacomo Begnoni, University of Leuven, Belgium
- 11:40 AM** Children's oro-facial muscular dysfunctions. Dangerous consequences on their oral and general health. Importance of their myofunctional treatment. Bedros Yavru-Sakuk. New York, USA
- 12:00 AM** **Lecture of Giorgio Fanò-Illic, Libera Università di Alcatraz, Gubbio (PG), Italy**
History and perspectives of translational myology
- 12:40** Lunch
- 02:00 PM** Oral care for the patients with xerostomia and hyposalivation in systemic diseases. Elena P. Ivanova, et al., University of Moscow, Russia Federation
- 02:20 PM** Orthopedic-orthodontic therapy of transverse expansion of the palate: is the adaptation of the masticatory muscles possible and in how long time? Francesca Ferrante, Beatrice Sfondrini, University of Pavia, Italy
- 02:40 PM** How and when does the performance of the masticatory muscles change during the treatment of periodontitis? Gaia Pellegrini, University of Milan, Italy-
- 03:00 PM** An interdisciplinary approach in the clinical and instrumental assessment of motor skills in athletes with disabilities. Elena Giannotti, Federico Ristoldo, HGP23, Italy
- 03:20 PM** Speech therapy in the dental office. Claudia Ferreira, Logos Academy, Milan, Italy
- 03:40 PM** Malocclusion and scoliosis what we know what we need to know. Sabina Saccomanno, Fabio Scoppa, Sabina Saccomanno, Alessio Pirino, Giuseppe Messina, San Raffaele University, Rome (Italy)
- 04:00** Coffee break **Conference Hall Paradise, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy**
- 04.20 PM** **Session IX: Muscle Imaging and Digital Health in Mobility Medicine**
Paolo Gargiulo, Ugo Carraro, Chairs
- 04:20 PM** **Lecture of Paolo Gargiulo and Riccardo Forni, University of Reykyavik, Iceland**
New direction of medical imaging transformation
- 05:00 PM** Redlan: an alternative method for analyzing electromyographic data in orthodontics. Lanfranco Vespertini, Bstat, DSc (Econ), Verona, Italy
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- 05:40 PM** Neurophysiology and advanced imaging to investigate muscular morphology and function in adolescent idiopathic scoliosis, Maria Chiare Maccarone et al., DNS, University of Padua, Italy
- 06:00 PM** Foot drop syndrome: neurophysiological and ultrasound approach in the evaluation of SPE deficit, Emanuele D'Andria, et al. Rehabilitation Unit of DNS, University of Padova, Padua, Italy
- 06:20 PM** **Lecture of Simona Boncompagni, University of Chieti, Italy: Calcium Entry Units (CEUs): dynamic intracellular junctions in skeletal muscle fibers**
- 07:30 PM** Dinner.

SATURDAY March 2, 2024

Conference Hall Paradise, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

09:00 AM Session X: LBI workshop on muscle rehabilitation

Sandra Zampieri, Feliciano Protasi, Chairs

- 09:00 AM** Mimicking short-term immobility and early rehabilitation in an animal model, Feliciano Protasi, University of Chieti, Italy
- 09:30 AM** Insights into muscle atrophy and sarcopenia: mechanisms and countermeasures, Antonio Musarò, University Sapienza of Rome, Italy
- 10:00 AM** Determinants and predictors of muscle mass, function and mobility: cross sectional study in young and old muscles, Sandra Zampieri, DiSCOG, University of Padua, Italy
- 10:30 AM** Water therapy: its place in rehabilitation and opportunities for optimisation, Nejc Sarabon, University of Primorska, Slovenia
- 11:00 AM** *Coffee break*
- 11:20 AM** Results of a new model of rehabilitative transitional care for geriatric patients, Vincent Grote, LBI Rehabilitation Research, Vienna, Austria
- 11:40 AM** Improved mentalizing is a protective factor against depressive symptoms and pain severity in patients with chronic rheumatic pain, David Riedl, LBI Rehabilitation Research, Vienna, Austria
- 12:00 AM** Is Isokinetic Dynamometry a useful assessment for physical function post- knee and hip arthroplasty? Ferdinand Prüfer, LBI Rehabilitation Research, Vienna, Austria
- 12:10 AM** Comparing rehabilitation programs using different types of outcome measures, Špela Matko, LBI Rehabilitation Research, Vienna, Austria
- 12:20 AM** Critical success factors in orthopedic rehabilitation - from the perspective of patients and doctors, Chiara Vetrano, LBI Rehabilitation Research, Vienna, Austria
- 12.30 AM** *Lunch*

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Line SATURDAY March 2, 2024

Conference Hall Grazia, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

09:00 Masterclass, Claudia Dellavia, Riccardo Rosati, Chairs

Masticatory muscles function maintenance and restoration in daily dentistry

In 1998, with the foundation of the Functional Anatomy Research Center (FARC) at the University of Milan, a dense research work about the function of the stomatognathic apparatus was born. Twentyfive years of rigorous application of the scientific method have led to the development of oral function measurement procedures, validated by several Universities through many scientific publications. A masterclass to understand the oral function measurement with Percentage Overlapping Coefficient (POC) processing and learn to translate functional information into reliable treatment plans for a quality daily clinic.

09:00 AM Instrumental recording of the function of the masticatory muscles: from the research laboratory to daily dentistry. Riccardo Rosati, Udine, Italy

10.30 AM Coordinated muscles as allies to increase the quality of daily dental rehabilitation. Piero Simeone, Rome, Italy

12.00 AM Questions and Answers

12.30 AM Closure

Location

Conference Hall Grazia, Hotel Petrarca,

Thermae of Euganean Hills (Padua) Italy - www.hotelpetrarca.it

Montegrotto Terme, Italy

1 March 2024 fee

100 euro on-site

Official language English; Italian translation available

2 March 2024 fee

200 euro on-site

Italian; ECM under construction

To obtain details and subscription forms for Masterclass:

riccardo@riccardorosati.eu

2024Pdm3 Registration and Accommodation: ugo.carraro@unipd.it

2024Pdm3 Payments to Hotel Petrarca: petrarca@hotelpetrarca.it

SATURDAY March 2, 2024

Conference Hall Paradise, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

- 02:00 PM** **Practical Activities III: Underwater physiotherapy & Home Full-Body in Bed-Gym,**
Helmut Kern, Maria Chiara Maccarone, Chairs
- 02:30 PM** **Underwater physiotherapy after knee replacement, Helmut Kern, LBI Rehabilitation**
Research, Vienna, Austria
- 03:00 PM** **Further optimizing Full-Body in Bed-Gym, Maria Chiara Maccarone, University of**
Padova, Padua, Italy
- 03:30 PM** **Discussants, To Be Announced**
13:50 AM Coffee break
- 04:00 PM** **SESSION XI: World Federation of Hydrotherapy (FEMTEC)**
Elena P. Ivanova, Stefano Masiero, Chairs
- 04:00 PM** **Balance control recovery by healing or by compensation in sensory and**
osteoarticular pathologies after hydrotherapy, Philippe Perrin & Marie-Catherine
Tallot, University Hospital of Nancy, Vandoeuvre-lès-Nancy & University of Lorraine,
France
- 04:30 PM** **Can optimized human home-based Full Body In-Bed Gym induce functional and**
structural improvements in octuagenarian muscles? Functional and structural
evidence. Daniele Coraci, et al., DNS, University of Padova, Padua, Italy,
- 04:50 PM** **Effect of intensive rehabilitation program in thermal water on a group of people with**
Parkinson's Disease: a longitudinal study, Lucrezia Tognolo, DNS, University of
Padova, Padua, Italy
- 05:00 PM** **Dynamic control of motor disorders in the early stages of Parkinson's disease, Kirill**
Terentev, University of Moscow, Russia
- 05:30 PM** **Asymmetry of the brain: an innovative test for left-handedness and leftness in**
neurorehabilitation, Igor Reverchuk et al., Immanuel Kant Baltic Federal University,
Kaliningrad, Russia
- 05:45 PM** **Mitochondrial dysfunction, stress and inflammation in neurodegenerative diseases,**
Polina Reverchuk et al., Immanuel Kant Baltic Federal University, Kaliningrad, Russia
- 06:00 PM** **Methodology for predicting the therapeutic effect of an area, Andrey Lobanov,**
University of Moscow, Russia
- 06:15 PM** **Additional pharmacological therapy for epilepsy with drugs unrelated to**
anticonvulsants, Georgiy Avakyan, University of Moscow, Russia
- 06:30 PM** **Personalized medical and psychological aspects of stress-related disorders in dental**
specialists, Sarkisov A.A., Reverchuk I.V., Zelensky V.A., Spitsyna A.V.
- 06:45 PM** **Conclusive remarks of Stefano Masiero, Rehabilitation Unit of DNS of the University**
of Padova, Padua, Italy
- 07:00 PM** **Ugo Carraro: Arrivederci, Auf Wiedersehen, Au revoir, Goodbye to the**
2025Padua 4 Days on Muscle and Mobility Medicine, February 26 to March 1, 2025.
Thermae of Euganean Hills (Padua), Italy
- 07:30 PM** **Dinner**

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INTERDEPARTMENTAL RESEARCH
CENTER OF MYOLOGY (CIR – MYO)
of the University of Padua, Italy***

ABSTRACTS of the 2024Pdm3

TUESDAY February 27, 2024

2024Pdm3 February 27 - Abstract 1

Introductory words for Charlotte Suetta's Lecture

Stefano Schiaffino
University of Padua, Italy
Email: stefano.schiaffino@unipd.it

Presentation on site. The author has asked to postpone the submission of the abstract.

2024Pdm3 February 27 - March 2, 2024

2024Pdm3 February 27 - Abstract 2

Lecture: Effects of bed rest and immobilisation in young and old individuals – NMES as a potential countermeasure

Charlotte Suetta,
University of Copenhagen, DK
Email: charlotte.suetta@regionh.dk

Presentation on site. The author has asked to postpone the submission of the abstract.

2024Pdm3 February 27 - March 2, 2024

2024Pdm3 February 27 - Abstract 3

Electrical stimulation in muscle dystrophy

Ines Bersch (1), Susanne Opel (1), Marie Alberty (1,2,3)

(1) International FES Centre[®], Swiss Paraplegic Centre Nottwil, Switzerland; (2) Swiss Paraplegic Research, Nottwil, Switzerland; (3) Albert Ludwigs Universität Freiburg, Switzerland.
Email: inesbersch@gmail.com

Muscle dystrophies belong to genetic disorders causing muscle progressive weakness and muscle degeneration. The genetic mutation responsible for a lack or dysfunction of proteins, known as the glycoprotein complex, leads to muscle weakness followed by degeneration of the muscles altering at least into connective tissue and fat.¹ The group of muscle

dystrophies is various so that there are still other forms caused by expression of toxic gene products in muscle fibers. Hence the overarching term muscular dystrophy encompasses a range of subgroups including Duchenne, Becker, congenital, myotonic, Emery-Dreifuss, facioscapulohumeral, oculopharyngeal, and limb-girdle muscular dystrophies and many more.¹ Clinical symptoms may include beside muscle weakness and denervation atrophy, muscle contractures, respiratory problems as pulmonary infections, and in some forms as the myotonic dystrophy also impairment of the endocrine system.² However, the overall prevalence including all types of muscle dystrophy ranges between 19.8 and 25.1 per 100.000 person a year.³ Since in muscle dystrophies also the lower motoneuron is affected, long pulse stimulation might be a treatment option to influence the progressive muscle wasting and degeneration.⁴ Clinical observation also shows hybrid forms in one and the same muscle group, where both an upper and lower motoneuron lesion occur. There is upcoming evidence that electrical stimulation could protect against dystrophin-associated-glycoprotein complex mutations.⁵ Nevertheless, to our knowledge there is no study up to date that describes the application and effects on long pulse stimulation and neuromuscular stimulation in terms of parameter choice, intensity, and volume of stimulation in humans with any form of muscle dystrophy. Therefore, the aim of our data analysis including clinical observation and experience in treating of five patients with long pulse electrical stimulation as well as neuromuscular electrical stimulation will be reported to provide a baseline for further investigation. A data analysis was conducted by reviewing the number of inpatients between 2020 and 2023 including length of hospitalization, gender, age and type of muscle dystrophy. In contrast, the number of patients with muscular dystrophy in 2023 who came as outpatients



Figure 1: Illustration of different electrical stimulation applications in patients with muscle dystrophy

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Table 1: Demographics of five patients who received electrical stimulation.

ID	Gender	Age	Diagnosis	Target
1	f	60	Muscle dystrophy type Goldbein	Improvement in walking distance/gait endurance
2	m	69	Myotonic dystrophy type 1	Improvement of swallowing function
3	f	71	Limb-girdle muscular dystrophy	Improvement in walking and muscle fatigue
4	f	45	facioscapulohumeral muscular dystrophy	Improvement in upper limb function
5	m	26	Muscle dystrophy - spinal muscle atrophy	Improvement in upper limb function and trunk stability

requesting treatment of their muscle weakness and atrophy with electrical stimulation was analyzed. In addition, these cases are described in detail how the stimulation schedule was performed and how stimulation, long pulse and neuromuscular electrical stimulation was administered (Figure 1). 37 people, 26 male 11 female, were hospitalized in mean 41.1 days \pm 48.3 days. Mean age was 44.2 years \pm 16.1 years. In 12 cases they were classified as myotonic dystrophy and the remaining 25 as muscle dystrophy not further specified. Five patients contacted the International FES Centre[®] directly on their own attempt to get an evaluation if the application of electrical stimulation might be meaningful in terms of reducing their muscular weakness and in one case to improve swallowing (Table 1). All five patients are currently under treatment with electrical stimulation one to two times a week. The treatment contains the stimulation in combination with functional exercises. The stimulation is conducted efferently and/or afferently. All patients report that their subjective well-being increased in terms of less fatigability, better swallowing, and increased strength and endurance. The effect is neither long-lasting nor does it lead to a persistent improvement.

In conclusion, electrical stimulation, including long-pulse stimulation as well as neuromuscular stimulation leads to a subjective reported short-term positive effect regarding fatigability, function as swallowing, muscle strength and endurance. Whether continuous application can delay the course of the disease should be investigated.

Key words: muscle dystrophy; long pulse stimulation; neuromuscular stimulation; lower motoneuron disease.

References

1. Mercuri E, Muntoni F. Muscular dystrophies. *Lancet*. 2013 Mar 9;381(9869):845-60. doi: 10.1016/S0140-6736(12)61897-2. PMID: 23465426.
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3. Theadom A, Rodrigues M, Roxburgh R, Balalla S, Higgins C, Bhattacharjee R, Jones K, Krishnamurthi R, Feigin V. Prevalence of muscular dystrophies: a systematic literature review. *Neuroepidemiology*. 2014;43(3-4):259-68. doi: 10.1159/000369343. Epub 2014 Dec 16. PMID: 25532075.

4. Bersch I, Mayr W. Electrical stimulation in lower motoneuron lesions, from scientific evidence to clinical practice: a successful transition. *Eur J Transl Myol*. 2023 Jun 8;33(2):11230. doi: 10.4081/ejtm.2023.11230. PMID: 37288875; PMCID: PMC10388603.
5. La G, Zhou M, Lim JY, Oh S, Xing H, Liu N, Yang Y, Liu X, Zhong L. Proteomics and Transcriptomics Analysis Reveals Clues into the Mechanism of the Beneficial Effect of Electrical Stimulation on Rat Denervated Gastrocnemius Muscle. *Cell Physiol Biochem*. 2019;52(4):769-786. doi: 10.33594/000000054. PMID: 30933441.

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2024Pdm3 February 27 - Abstract 4

Surface Electrostimulation stops denervated muscle atrophy in facial paralysis

Krauss J (1,2), Meincke G (1,2), Geitner M (1,2), Arnold D (1,2), Kutenreich A (1,2), Büchner T (4), Denzler J (4), Guntinas-Lichius O (1,2,3), Mayer W (5), Volk G F (1,2,3)

(1) ENT-Department, Jena University Hospital, Jena, Germany; (2) Facial-Nerve-Center, Jena University Hospital, Jena, Germany; (3) Center for Rare Diseases, Jena University Hospital, Jena, Germany; (4) Computer Vision Group, Friedrich Schiller University Jena, Germany; (5) Medical University Vienna, Center for Medical Physics and Biomedical Engineering, General Hospital Vienna, Austria.

Email: fabian.volk@med.uni-jena.de

Sparse evidence of the therapeutic potentialities of surface electrostimulation (ES) for the treatment of facial paralysis has been published so far. Especially studies containing objective imaging methods for paralysis quantification are currently required. Facial muscles as principal target of ES can be directly quantified via ultrasound, a swiftly feasible imaging method. Our study represents one of the few systematic evaluations of this approach within patients with complete unilateral facial paralysis.¹⁻³ We used the established ultrasound protocol

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for facial muscles to predict therapeutical effects on patients with facial paralysis. ES-parameters were adjusted during the first visit and confirmed/adapted every month thereafter. At each visit patients additionally underwent needle-electromyography to verify if the paralysis would still be present as well as ultrasound imaging of the facial muscles. Stimulation was carried out at home for 20 minutes twice a day on the paralytic side of the patients' faces. In total, 15 patients with complete one-sided peripheral facial paralysis were recruited (medium 53 years, min. 25, max. 78; 8 female, 7 male). They performed surface ES for a maximum of one year. The assessment of ultrasound imaging indicate that paralytic electro-stimulated zygomaticus muscle increases during the first month of ES, while control muscles outside the focus of ES further decreases in cross-sectional area compared. Photo assessment, but also patient related outcome measures (PROMs) support this positive effect of during ES. In conclusion, Intense Electrostimulation can stop the denervation atrophy of facial muscles. Hence, the increase of ultrasound quantified muscle cross-sectional areas, but also photo and PROMs in facial paralysis, provides a clear indication of ES. Never the less, a randomized controlled study to compare ES with e.g. sham stimulation, is needed.

Key words: muscle atrophy; facial paralysis; Surface Electrostimulation.

References

- 1 Kurz A, Volk GF, Arnold D, Schneider-Stickler B, Mayr W, Guntinas-Lichius O. Selective Electrical Surface Stimulation to Support Functional Recovery in the Early Phase After Unilateral Acute Facial Nerve or Vocal Fold Paralysis. *Front Neurol.* 2022 Apr 4;13:869900. doi: 10.3389/fneur.2022.869900. PMID: 35444611; PMCID: PMC9013944.
- 2 Arnold D, Thielker J, Klingner CM, Puls WC, Misikire W, Guntinas-Lichius O, Volk GF. Selective Surface Electrostimulation of the Denervated Zygomaticus Muscle. *Diagnostics (Basel).* 2021 Jan 28;11(2):188. doi: 10.3390/diagnostics11020188. PMID: 33525522; PMCID: PMC7912406.
3. Mastryukova V, Arnold D, Güllmar D, Guntinas-Lichius O, Volk GF. Can MRI quantify the volume changes of denervated facial muscles? *Eur J Transl Myol.* 2020 Apr 1;30(1):8918. doi: 10.4081/ejtm.2019.8918. PMID: 32499901; PMCID: PMC7254417.

Sponsored by DFG GU-463/12-1, DEGUM and IZKF.

2024Pdm3 February 27 - March 2, 2024

2024Pdm3 February 27 - Abstract 5

NMES in skin disorders

Giovanna Albertin, Human Anatomy, DNS, University of Padua, Italy

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Presentation on site. The author has asked to postpone the submission of the abstract.

2024Pdm3 February 27 - March 2, 2024

2024Pdm3 February 27 - Abstract 6

Paired stimulation for denervated muscle in persons with SCI: A proposed study

Ashraf Gorgey

School of Medicine, Virginia Commonwealth University, Richmond, VA, USA

Email: agorgey@gmail.com

Presentation on line. The author has asked to postpone the submission of the abstract.

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2024Pdm3 February 27 - Abstract 7

Perspectives of over 20 years of FES to treat equine muscle spasms and the potential crossover into humans

Sheila Schils

EquiNew, River Falls, Wisconsin, USA

Email: sbschils@EquiNew.com

Presentation on line. The author has asked to postpone the submission of the abstract.

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2024Pdm3 February 27 - Abstract 8

Towards patient-controlled skeletal muscle pacemaker for SCIs

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Presentation on line. The author has asked to postpone the submission of the abstract.

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2024Pdm3 February 27 - Abstract 9

Electric stimulation for Bell's palsy

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Bell's palsy is the most common cause of facial paralysis, affecting one in every 60 people in their lifetime.¹ Transcutaneously applied selective electrical muscle stimulation could potentially accelerate recovery from Bell's palsy but this intervention remains controversial. Studies have shown benefit, but concerns for lack of efficacy and potential for worsening synkinesis remain. During this presentation we will review current evidence of electric stimulation for facial paralysis, and discuss our recent prospective controlled trial comparing outcomes at initial recovery and six months later with selective electrical muscle stimulation and usual physical therapy versus usual physical therapy alone in adults with acute Bell's palsy. Monophasic pulsed exponential waveform was used. Participants in the electrical stimulation group achieved maximal recovery twice as fast as the control group (2.5 weeks versus 5.2 weeks) with no significant



Stimulation was applied transcutaneously with a digital technique where the positive electrode was placed on the ipsilateral neck of the patient and the negative electrode was placed on the dominant forearm of the treating physical therapist. Stimulation was provided by the therapist's fingers being applied to treatment locations on the patient's face.

Reproduced with permission from Di Pietro A, et al.²

differences in facial function or synkinesis between groups at any time point. Strengths and limitations of the study will be discussed. Finally, the electrical stimulation technique used in the study will be demonstrated with a volunteer patient. Electrical stimulation was applied transcutaneously with an indirect digital technique where the positive electrode was placed on the ipsilateral neck of the patient and the negative electrode was placed on the dominant forearm of the treating physical therapist.² The current had a monophasic exponentially rising pulsed waveform, with a pulse width >30ms, with pulse width and current amplitude adjusted to optimize comfort and muscle contraction strength and selectivity.

Key words: electrical stimulation, Bell's palsy.

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2024Pdm3 February 27 - Abstract 10

FES for Denervated Degenerating Muscles (DDM): ten years of experience

Helmut Kern (1,2), Ugo Carraro (3,4,5)

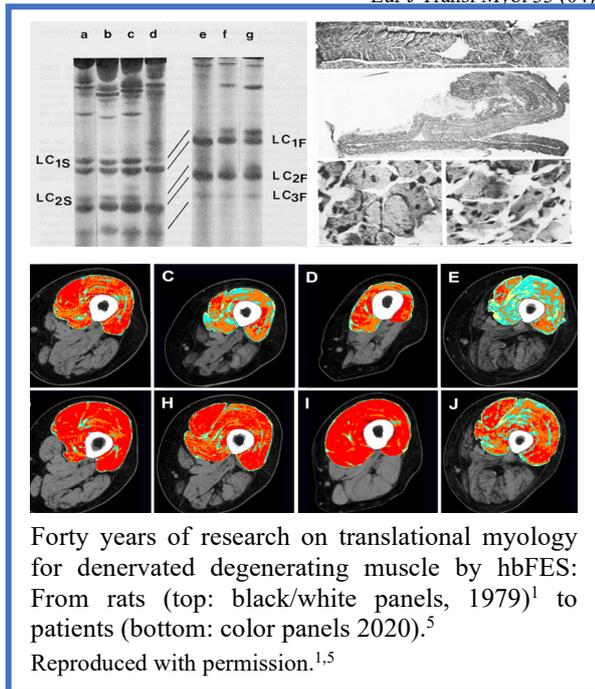
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We will start from the beginning of our research activities and the serendipitous events of Ugo's and Helmut's dedication to permanent denervation of muscles and their electrical stimulation in animal models and in human patients. After years of basic research on long-term muscle denervation and their electrical stimulation in rat models,¹ I met Helmut Kern at one of the Vienna

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Workshops on Functional Electrical Stimulation (FES), in 1998, and then in 1999 when he came to see me at the Department of Biomedical Sciences of the University of Padua during one of his stays at the Hotels in Montegrotto Terme (Padua), Italy. He was and is fanatic of the warm pools and the ups and downs of the Euganean Hills where he pedaled under clear sky. Helmut had brought his Rehabilitation thesis, which described experiences of a very young Rehabilitation Specialist, who had treated the first cases of implantation of the Vienna FES electrostimulators in paraplegic patients. He asked for my opinions and offered collaborating to collect more solid evidence of muscle improvements even in the worst cases, those of patients with permanent denervation of the legs. My immediate response was: Dear Helmut, could you collect biopsies from the muscles of rehabilitating legs? Because he was very optimistic, a long-standing partnership began almost immediately and continues to date with undisputable clinically-relevant results.²⁻⁵ Since we could and can provide strong evidence-based clinical results, they attracted some interest, but they remained a unique case, possibly related with the fact that Complete Conus Cauda Syndrome is in the realm of rare diseases.

Fortunately, others are brave enough to try electrical stimulation in other more frequent clinical cases of human muscle denervation with very interesting preliminary results.⁶⁻¹⁰

Key words: permanent muscle denervation; electrical stimulation; hbFES for DDM.

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2024Pdm3 February 27 - Abstract 11

Conclusive remarks

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 February 28 - Abstract 12

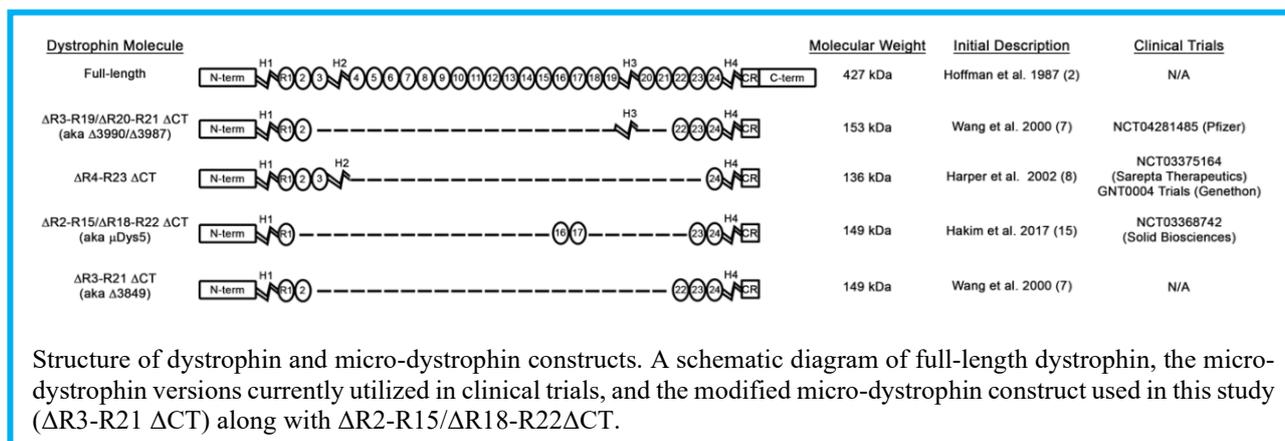
Progress toward designing a micro-dystrophin to rescue all striated muscles

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Adeno-associated viruses (AAVs) containing versions of truncated dystrophin (micro-dystrophins) are being delivered to patients with Duchenne muscular dystrophy (DMD) in clinical trials. DMD is a progressive, childhood onset muscle wasting disease caused by mutations in the DMD gene that result in the loss of dystrophin protein in all muscle types.¹ These clinical gene therapies aim to overexpress a truncated version of dystrophin in striated muscle capable of achieving partial correction of the disease. We have examined this strategy with all of the micro-dystrophins shown in Figure 1, using at severe mouse model of DMD, the D2.mdx mouse.²⁻⁴ We administered doses of AAV comparable to those used in the clinical trials. Significant correction of the limb skeletal muscle disease is observed, which slows, but does not halt muscle disease progression. However, a lethal acceleration of cardiac disease progression occurred with two of the micro-dystrophins, while one had little or no impact on the heart, and one did not express well and had no impact. The detrimental impact on the heart appears to be caused by high levels of micro-dystrophin that result in competition between micro-dystrophin and utrophin at the cardiomyocyte membrane and by excessive protein accumulation. The micro-dystrophin with no cardiac impact does not outcompete utrophin to the same extent as the deleterious constructs. While the significance of these observations for patients currently being treated with AAV-micro-dystrophin therapies is unclear, since the expression levels in their hearts are unknown, it suggests that micro-dystrophin treatments for the heart may need to be carefully titrated, and potentially dissociated from treatment for skeletal muscle, to achieve optimal benefits for both types of muscles. Additionally, different elements of dystrophin may need to be included to rescue the heart. To address this last point, we have constructed novel micro-dystrophin constructs and have identified elements that are beneficial for the cardiac disease.



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Key Words: Duchenne muscular dystrophy, AAV, gene therapy, cardiomyopathy

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Skeletal muscle response after treatment in spinal muscular atrophy

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Spinal Muscular Atrophy (SMA) is caused by the mutation of the survival of motor neuron 1 (SMN1) gene and reduced SMN protein expression. Three non-curative treatments have been approved for SMA to date, significantly revolutionizing the life of the patients and their care. Despite ensuring ventilation free survival and great locomotion improvements, these therapies engage a variable response in patients particularly in the rescue of the skeletal muscle defects. Unfortunately, only few datasets are available from treated SMA patient muscle limiting our understanding of the effect of the treatments on the pathological features of the SMA muscle. To characterize the molecular underpinning of SMA muscle and its response to treatment, we collected paravertebral muscle from SMA Type II patients (n=8) after treatment with an antisense oligonucleotide (Nusinersen) and age matched controls (n=7) and performed RNA-sequencing. This analysis revealed that there are 2 distinct groups of

patients with distinct molecular fingerprints. The first group, which we will call SMAII-A, had an overall transcriptional landscape similar to that of their age matched controls (5/8 samples). The second, which we will call SMAII-B (3/8 samples), had a transcriptional profile that was highly different from the controls. Interestingly, the clustering obtained with this method defined molecular “responders” and “non-responders” groups which correlated with the clinical locomotor scales.

Our study reveals that the Nusinersen treatment elicits a variable skeletal muscle response in SMA type II patients. We believe that the SMAII-B patients would potentially benefit from a combined therapy with an SMN-independent approach to favor a more efficient muscle functional rescue.

Key words: skeletal muscle; spinal muscular atrophy; response after treatment.

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2024Pdm3 February 28 - Abstract 14

Satellite Cell-opathies and how to find them

Massimo Ganassi, Peter S. Zammit

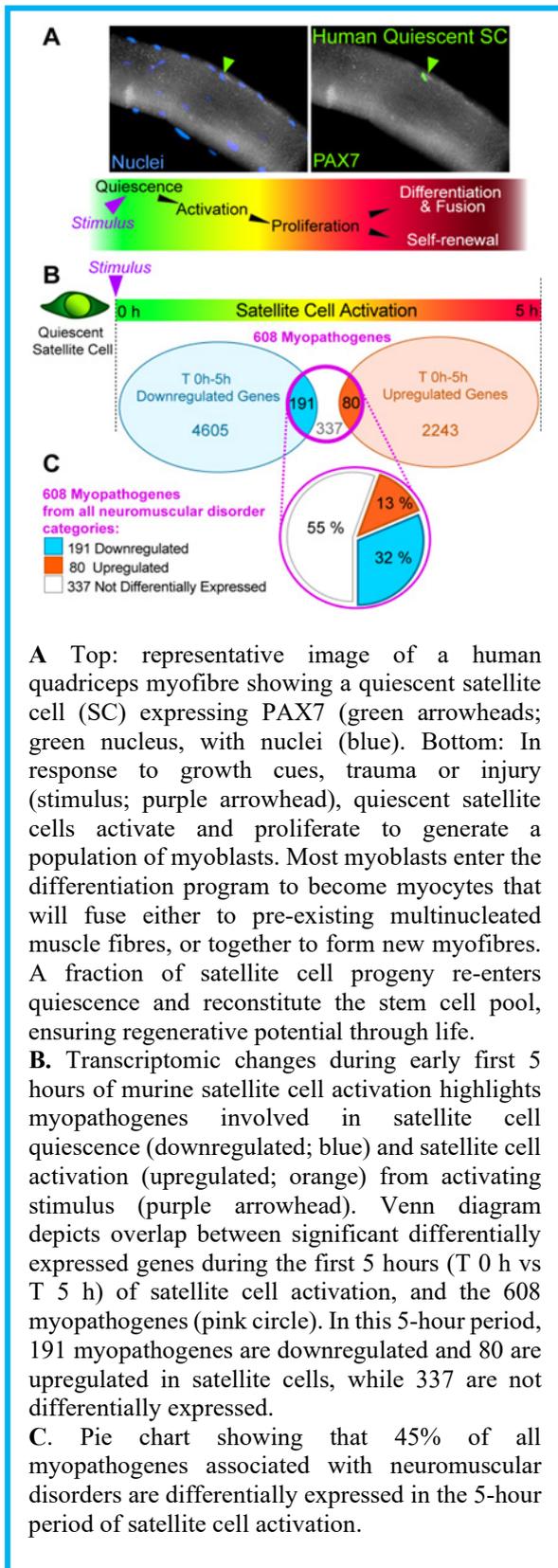
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Skeletal muscle health relies on resident muscle stem cells called satellite cells, which enable life-course muscle maintenance, hypertrophy and repair (Figure 1A). Muscle plasticity gradually diminishes in diseases like muscular dystrophies and congenital myopathies, suggesting compromised satellite cell function.

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We have recently defined a new class of disease we termed Satellite Cell-opathies, where the underlying genetic mutation also impairs the function of a gene (myopathogene) directly regulating satellite cell biology, and so impairing muscle maintenance/repair. We define Primary Satellite Cell-opathies as conditions where genetic mutations directly affect only satellite cell function: generally characterised by congenital onset, hypotonia, involvement of respiratory, trunk and facial muscles. Examples include mutations in PAX7 causing P progressive Congenital Myopathy with Scoliosis and in MYMK or MYMX causing Carey-Fineman-Ziter Syndrome. In contrast, Secondary Satellite Cell-opathies originate from pathogenic mutations directly impacting on both satellite cells and muscle fibres, leading to more heterogeneous clinical presentation in terms of onset and muscle groups affected. Examples are LMNA mutations underlying laminopathies and alterations at the D4Z4 macrosatellite in facioscapulohumeral muscular dystrophy.¹ A central issue is to determine if a pathogenic mutation in a myopathogene directly perturbs satellite cell function. We deploy transcriptomic analysis and comparison to assess whether genes associated with all classes of hereditary neuromuscular conditions, including those with mainly neurogenic and cardiac involvement, are differentially expressed during adult satellite cell activation (Figure 1B). Next, we determine whether such myopathogenes are controlled by PAX7, a master regulator of satellite cell myogenesis. Finally, we consider satellite cell numbers and function in the associated neuromuscular disease and animal models. Using our multimodal approach, we found that nearly 50% of myopathogenes are expressed in satellite cells (Figure 1C), indicating that satellite cell dysfunction may represent a common pathological mechanism across neuromuscular disorders.²

Key words: satellite cell-opathies; neuromuscular disorders; muscle regeneration; muscle stem cells; skeletal muscle.

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2024Pdm3 February 28 - Abstract 15

Cancer cachexia and precision medicine

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 February 28 - Abstract 16

Mitochondria network dynamics in human cancer cachexia

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Cachexia is a hypercatabolic syndrome characterized by skeletal muscle loss in the context of a chronic inflammatory response that can occur in the setting of advanced cancer. Across malignancies, cachexia is highly prevalent in patients with gastrointestinal cancers and the loss of muscle mass and strength has been shown to be a key predictor of poor outcomes.¹ Very recently, denervation-induced atrophy and neuromuscular junction (NMJ) disarrangement received attention as new pathogenetic mechanisms responsible for skeletal muscle wasting in cancer cachexia.² Our previous study identified denervation muscle atrophy and high circulating levels of biomarkers related to NMJ disarrangement in skeletal muscle biopsies and sera from pre-cachectic and cachectic patients affected with pancreatic and colorectal cancers.³ In mice models of cancer cachexia degeneration of the mitochondrial network leading to a loss of mitochondrial function has been demonstrated,⁴ disrupting skeletal muscle health leading to muscle atrophy, but data on mitochondrial morphology and dynamics relatively to denervation in skeletal muscles from cachectic human patients are missing. To close these gaps, we decided to perform a human study on skeletal muscles from patients affected

with distinct tumors focused on morphological and ultrastructural features of denervation and mitochondrial network remodeling as emerging pathogenetic mechanisms underlying mitochondrial dysfunction and loss of skeletal muscle mass in cancer cachexia.

Key words: cancer cachexia; denervation; skeletal muscle loss; mitochondria.

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Neuromuscular coordination: from birth to adulthood

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Muscle properties change drastically postnatally. Both fast and slow muscles initially exhibit similarly slow contraction, which speeds up over the first few weeks after birth.¹ Polyneuronal innervation also gradually subsides.² I will briefly review studies showing how the neural control of muscles adapts to changing muscle properties. With development, the amplitude and shape of motor neurons action potentials change, due to changes in several biophysical parameters such as the membrane resistance and capacitance, and the maximum firing frequency increases. These changes occur earlier in cervical motor neurons than lumbar motor neurons, in parallel with the earlier arrival of cortico-spinal descending pathways at cervical than lumbar cord. In neonates, motor neurons discharge highly synchronous action potentials.³ This is quantified by the temporal cross-correlation and the coherence in the frequency domain (the delta band at 0 to 5 Hz). High synchrony compensates for the slow contraction times of neonatal muscles and is responsible for fast movements. Motoneuron synchronization is due to common synaptic inputs from premotor interneurons of the central pattern generators and from afferent feedback. Contribution to synchronization also comes from electrical gap-junctions between motoneurons. Newborns cannot sit nor stand, yet they are able to step automatically on ground if supported. This innate ability depends on the presence of basic spinal modules of neuromuscular control, which are shared across mammals and birds.⁴ With maturation, the native motor modules split and generate new modules, so that the complexity of commands increases while variability decreases.⁵ The maturation process is slow in altricial species (such as the human) or fast in precocial species (such as the ungulates), the overall time taken to develop independent locomotion since conception being proportional to brain size. Conserved evolutionary features coexist with innovations in each animal species. In adult humans, the control of erect bipedal locomotion requires brief activations of leg muscles to accommodate discrete arm movements (such as reaching and grasping an object) within rhythmic locomotion.

Key words: motor primitives; muscle synergies; polyinnervation; gap junctions.

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2024Pdm3 February 28 - Abstract 18

Advancing assessment and diagnostic with the use of virtual histology and 3D techniques

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Advancing assessment and diagnostic techniques in healthcare has been made possible with the use of virtual histology and 3D techniques. Among these methods, 3D Printing (3DP) has emerged as a well-known and established technology. Its applications in healthcare have become increasingly intriguing and challenging, gaining attention and value in recent years. With the ability to acquire medical images, such as MRI and CT scans, and apply specific scanning protocols, 3DP in healthcare has proven to be a potential solution and support for numerous clinical problems. By utilizing the segmentation of regions of interest and specific technology, clinicians can create 3D models of

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anatomical structures. These models have various applications, including visualizing and preparing for surgical procedures, enhancing communication between patients and doctors, and serving educational purposes by displaying complex pathological anatomies in a novel way. Today, there are under development new applications such as Virtual reality and augmented reality showing their great potentials for improving planning and clinical training.. The Icelandic model have been inspiring several institutions in Europe and in collaboration with over 40-word wide professionals we recently edited a book entitled Handbook of Surgical Planning and 3D Printing: Applications, Integration, and New Directions to establish a point of reference for 3D printing practice in Healthcare.^{1,2}

Key Words: advancing assessment and diagnostic; virtual histology; 3D techniques.

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2024Pdm3 February 28 - Abstract 19

Motor unit alteration following MBNL functional loss in myotonic dystrophy

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 February 28 – Abstract 20

Unraveling the effects of Time Restricted Eating on inflammation and related biological processes

Stephen Anton (1,2)

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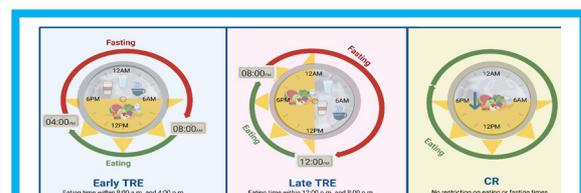
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Time-restricted eating (TRE) is a type of intermittent fasting in which food intake is confined to a particular time window each day. This approach has recently garnered substantial attention as a dietary intervention due to its potential health benefits, such as weight loss and improvement of metabolic disease risk factors. During the past couple of decades, TRE has been recognized to induce a number of health benefits, such as weight loss and improvement of metabolic disease risk factors, particularly in adults with obesity. Findings from preclinical studies,^{1,2} and emerging findings from human studies,³ indicate that TRE imparts many of these health benefits by influencing a number of biological processes including autophagy,¹⁻³ inflammatory responses,⁴ and gut microbiota.⁵ There remains some debate,⁶ however, whether many health benefits attributed to TRE are due to unintentional calorie restriction or the longer fasting period. Others have suggested that TRE can help to align circadian rhythms,⁷ and that the interplay between circadian molecular metabolism with TRE is what underlies the numerous health benefits. The focus of this presentation will be on unraveling the effects of TRE on inflammation and related biological processes by examining the influence that factors, such as calorie restriction, time of day in which food is consumed, and daily fasting duration have in influencing study findings. Key words: Time-restricted eating; inflammation; circadian rhythms.

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Early and Late Time Restricted Eating (TRE) schedules based on studies conducted in humans. Early TRE windows typically end by 4:00 pm (16.00 h) or before, whereas late TRE windows end after 6:00 pm (18.00 h), permitting an evening meal. The typical eating window duration in clinical trials ranges from 4 to 12 hours. In contrast, in studies involving calorie restriction (CR), the eating window is not restricted but calorie intake is typically reduced by 20-30% of baseline intake.

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IGF-I from fibroadipogenic progenitors is a critical modulator of muscle regeneration

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Skeletal muscle regeneration requires coordinated actions of multiple cell populations, including Fibro-Adipogenic Progenitors (FAPs). FAPs are mesenchymal stem cells that are located between myofibers and adjacent to capillaries¹. In the past decade, it has been established that FAPs are the predominant progenitor stem cells generating adipocytes and fibroblasts and are required for muscle regeneration². Insulin-Like Growth Factor-I (IGF-I) is a hormone that contributes significantly to skeletal muscle regeneration³. Importantly, FAPs are a prominent producer of IGF-I in skeletal muscle during acute muscle regeneration. However, the function of IGF-I from FAPs remains poorly understood. To understand the function of IGF-I produced from FAPs, we developed a FAP-specific *Igf1* Deletion mouse (FID) using *Pdgfra-Cre-ERT2 x Igf1 fl/fl x Rosa26EYFP* mouse lines. Mice lacking the *Igf1 fl/fl* allele served as wildtype (WT) controls. Adult mice were treated with tamoxifen by IP injections for 5 days to activate Cre recombinase. Unilateral injections of BaCl₂ were used to acutely injure tibialis anterior muscles (Fig 1A). Fiber size was determined by laminin immunostaining⁴, and was highly significant 7 and 14 days post-injury (dpi), where median fiber cross-sectional areas were 15-30% smaller in male and female FID muscles (Fig. 1B), suggesting a paracrine effect of FAP IGF-I on regenerating fibers. This was confirmed by reduced MyoD expression, and reduced Pax7-positive cells early in regeneration. Next, 3 rounds of repeated damage spaced 21 days apart caused muscles from female WT mice to increase by >40%, whereas those from female FID mice increased by only ~22%, supporting the paracrine actions of FAP IGF-I on muscle

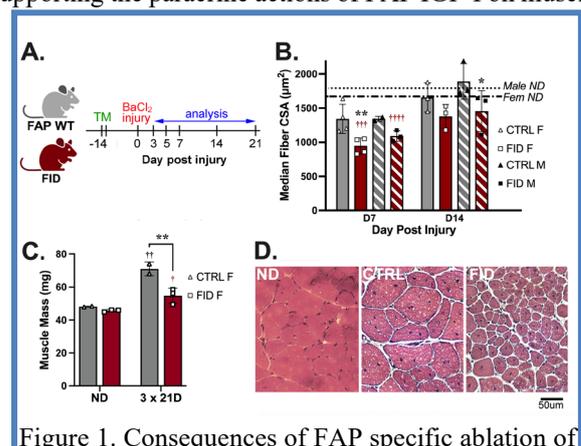


Figure 1. Consequences of FAP specific ablation of *Igf1*. A. Study design for acute injury experiments. B. FID mice have reduced fiber size during muscle regeneration. C. Repeated injury exacerbates phenotype of impaired muscle hypertrophy. D. H&E staining of muscle sections in non-damaged (ND) and repeated damage 21 days apart in WT (CTRL) and FID muscles.

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cells (Fig. 1C-D). To evaluate the autocrine actions of FAP IGF-I, we examined ECM content and PDGFR α -positive cells during regeneration. Muscle sections from 21 dpi stained with picrosirius red revealed decreased collagen in regenerating muscles from FID mice. Further, 3 bouts of damage spaced 7 days apart increased FAP presence in WT muscles, but their appearance was blunted in FID muscles. FAPs were visible near blood vessels in FID muscles, but they did not adopt the extended morphology around regenerating fibers observed in WT muscles. These data reveal an autocrine need of FAP IGF-I for proliferation and/or survival. Indeed, impaired FAP survival was clear when FAPs from FID muscles were extracted for primary cultures: expansion of FAPs lacking Igf1 expression was severely reduced. Altogether, we conclude that IGF-I from FAPs is required for efficient skeletal muscle regeneration, intercellular interaction between FAPs and muscle cells, and survival of FAPs themselves.

Key words: muscle regeneration; paracrine IGF-I effects; autocrine IGF-I effects.

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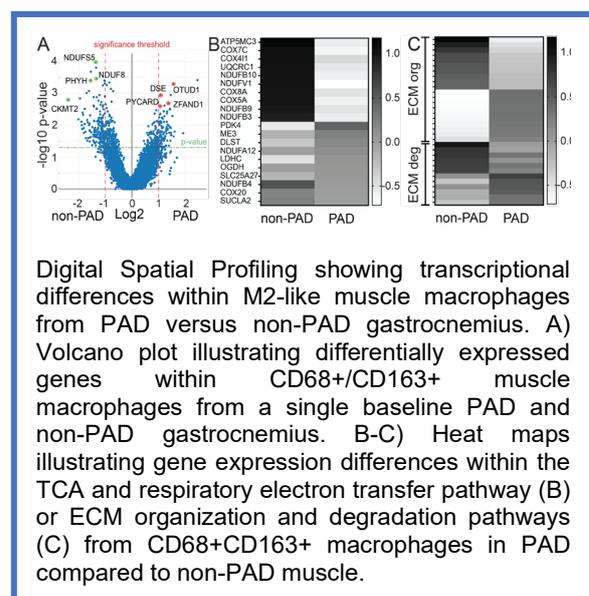
2024Pdm3 February 28 - Abstract 22

Immunomodulation of skeletal muscle regeneration: muscle macrophages and beyond

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Skeletal muscle regenerative capacity declines with aging and diseases like peripheral artery disease (PAD). Macrophages have documented roles in muscle regeneration and regrowth¹. In fact, evidence suggests modulating macrophage phenotype in aged muscle can restore regenerative capacity and functional recovery following disuse². However, relatively little is known about specific macrophage functions and cellular interactions within aged or diseased human muscles. This is partially due to methodological limitations when working with human biopsies: little contribution of protein/nuclei from macrophages in whole muscle analytes and low macrophage numbers following isolation from small tissue biopsies. We, and others, have shown greater M2 macrophages in both aging² and PAD³ muscle; although, the physiological impact of this phenotypic shift is not fully understood. Here, we present preliminary results obtained using the Nanostring GeoMX digital spatial profiler (DSP) with whole transcriptome atlas (WTA). Macrophage markers (CD68/CD163) were used to select M2 macrophages within gastrocnemius muscle and transcriptome profiling was performed. CD68+/CD163+ muscle macrophages from PAD showed higher expression of genes related to inflammation (OTUD1, PYCARD) and apoptosis (DSE) and lower expression of mitochondria related genes compared to non-PAD (Figure A). Additionally, altered expression of genes encoding TCA cycle components and regulators of extracellular matrix were observed in M2 macrophages from PAD muscle compared to non-PAD (Figure B & C). These findings suggest PAD results in metabolic changes within tissue resident muscle macrophages. Furthermore, these changes may contribute to reported increases in fibrosis, muscle pathology and functional decline with PAD. Moreover,



Digital Spatial Profiling showing transcriptional differences within M2-like muscle macrophages from PAD versus non-PAD gastrocnemius. A) Volcano plot illustrating differentially expressed genes within CD68+/CD163+ muscle macrophages from a single baseline PAD and non-PAD gastrocnemius. B-C) Heat maps illustrating gene expression differences within the TCA and respiratory electron transfer pathway (B) or ECM organization and degradation pathways (C) from CD68+CD163+ macrophages in PAD compared to non-PAD muscle.

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prior studies have shown bone marrow age affects resident muscle macrophage phenotypes⁵. Thus, shifts toward inflammatory/Th-1 responses with aging (“Inflammaging”), or disease, may exacerbate metabolic changes in muscle resident macrophages. Understanding metabolic changes in muscle macrophages with aging, as well as changes in circulating immune populations, may uncover new immunomodulatory drugs able to restore regenerative capacity in muscle with aging or disease.

Key words: skeletal muscle macrophages; immunomodulation; muscle regeneration; inflammaging.

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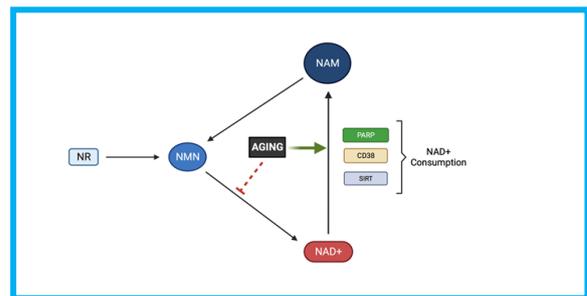
Clinical Trials Investigating Supplementation with Nicotinamide Riboside and Nicotinamide Mononucleotide in Older Adults

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Organismal aging is associated with numerous biological changes- one of which is a decrease in cellular and tissue-specific levels of nicotinamide adenine dinucleotide (NAD⁺). Several preclinical studies have shown a decrease in NAD⁺ synthesis and content which may contribute to pathologies mediated by changes in sirtuin expression and activity as well as DNA repair deficits.



These pathologies include glucose dyshomeostasis, non-alcoholic fatty liver disease (NAFLD), atherosclerosis, and Alzheimer’s disease (AD). Given this wide range of conditions associated with a decline in NAD⁺ content, there has been much recent interest in supplementation with compounds that can increase cellular NAD⁺ levels. Specifically, Nicotinamide Riboside (NR) and Nicotinamide Mononucleotide (NMN) are both NAD⁺ intermediates that have been shown to increase NAD⁺ levels in preclinical studies and randomized controlled trials (RCTs). At this time, there have been 13 RCTs investigating the use of NR in humans and 8 RCTs investigating NMN. These RCTs show that there is a dose-dependent increase in NAD⁺ with both NR,^{1-8,11,15,18-19} and NMN supplementation,^{9-10,12-13,16,20-21} however, the clinical significance of these trials is variable. In these trials, NR supplementation did not improve mitochondrial function,^{5,17} insulin sensitivity,^{6-7,17} or glucose oxidation;^{7,17} however, one trial reported a reduction in Aβ₄₂, a biomarker associated with AD.¹⁹ Another trial reported a reduction in alanine aminotransferase (ALT) in patients with NAFLD.⁴ As for NMN, no trials report improvements in cardiovascular or metabolic parameters;^{9-10,12,20} however, two trials demonstrated improvements in submaximal

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exercise performance.^{14,20} Thus, emerging findings from RCTs indicate NR and NMN have potential to address a decline in NAD⁺ synthesis and/or a greater need for NAD⁺ for optimal cellular function with aging. More RCTs are needed to establish whether NR or NMN supplementation can truly improve clinical outcomes such as walking speed, cognition and vascular functional assessments in older adults.

Key Words: nicotinamide riboside; nicotinamide mononucleotide; clinical trials; function; aging.

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Mediators of youthfulness in skeletal muscle

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Presentation on site. The author has asked to postpone the submission of the abstract.

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GDF5-based therapeutic approach to counteract age-related muscle wasting

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Sarcopenia is a disease defined as progressive age-related loss of muscle strength, function and mass, which results in increased mortality. Several mechanisms have been proposed to explain the onset and progression of sarcopenia, however, some pathophysiological aspects are still not very well understood and no cure has been established to date. Our previous work demonstrated that GDF5 (Growth Differentiation Factor 5) overexpression in old mouse prevented muscle mass decline, although a deeper report on the mechanisms and consequences of GDF5 implement on aged muscle was missing.

Here, we demonstrate that GDF5 overexpression in muscle during aging induces muscle mass gain and improves neuromuscular connectivity and endplate morphology. In addition, we present the characterization of the cellular and molecular effects of GDF5 in muscle during aging and show its “rejuvenating signature”. Based on this proof of concept, we defined a cutting-edge therapeutic approach describing how the treatment with the recombinant GDF5 protein is able to counteract the age-related skeletal muscle wasting in mice and might have a strong curative potential on humans.

Key Words: muscle; counteracting age-related wasting; GDF5-based therapy.

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2024Pdm3 February 28 - Abstract 26

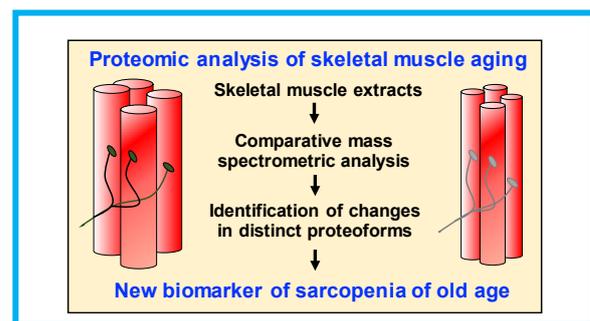
Proteomic profiling of fibre type shifting in aged skeletal muscles

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A large spectrum of physical ailments is associated with the natural aging process, including sarcopenia, which is defined as the age-related decline in both muscle mass and contractile strength. Sarcopenia of old age increases the risk of frequent falling, poor balance and impaired mobility. Thus, mobility medicine plays a crucial role in combatting progressive muscle wasting in the elderly, including counter measures in bed-ridden patients using home-based full-body in-bed gym based exercises. Lifelong physical activity was clearly shown to have beneficial effects on the neuromuscular system. Our laboratory has applied comparative proteomics to study sarcopenia of old age using both animal models and human biopsy specimens. The findings from mass spectrometric surveys agree with the pathophysiological concept that sarcopenia is based on multi-factorial mechanisms and that fast-to-slow transitions and considerable metabolic changes occur in senescent skeletal muscles. Novel proteomic biomarkers of aging can be useful for improving diagnostic/prognostic procedures and therapeutic monitoring of sarcopenia.



Key Words: Aging; muscle aging; myofibre; sarcopenia of old age, senescence.

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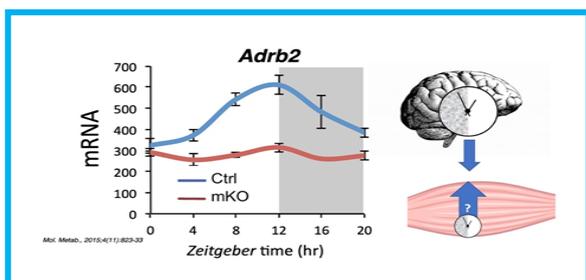
2024Pdm3 February 28 - Abstract 27

Circadian Catecholamine Sensitivity: Does Time Matter?

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Circadian clocks control metabolism and energy homeostasis, and chronic circadian disruption is a risk factor for metabolic diseases, including type 2 diabetes. To investigate the functional role of the skeletal muscle clock we generated conditional and inducible mouse lines with muscle-specific ablation of *Bmal1* (mKO), an essential clock gene. We previously reported mKO mice display normal 24-hr feeding and activity rhythms compared to wildtype littermates, yet mKO skeletal muscles show dramatically altered 24-hr gene expression, impaired insulin sensitivity, and major changes in glucose, lipid, amino acid and protein metabolism. Hormones and metabolites, including the



catecholamines adrenaline and noradrenaline can modulate circadian genes and synchronize clocks in the periphery. We found that transcripts coding for adrenergic receptor $\beta 2$ (*Adrb2*), the main catecholamine receptor in skeletal muscle, oscillate ~2-fold over 24-hr and peak at the transition from sleep to awakening when circulating catecholamines are also highest. To investigate whether $\beta 2$ -adrenergic receptors ($\beta 2$ -AR) also oscillate at a functional level, we measured specific binding of $\beta 2$ -AR in membrane fractions isolated from mouse quadriceps across 24-hr. We found membrane-bound $\beta 2$ -AR followed 24-hr *Adrb2* mRNA expression patterns by ~6hr, with lowest levels during the day, when mice are normally asleep and fasting, and ~3-fold higher membrane-bound $\beta 2$ -AR at night, when mice are normally awake, active and feeding. 24-hr *Adrb2* mRNA oscillation is completely abrogated in muscles from muscle-specific *Bmal1* knockout mice, including an inducible model in which muscle *Bmal1* is inactivated during adulthood. In addition, some effects of acute $\beta 2$ -AR stimulation were severely blunted in mKO muscles, as shown by decreased phosphorylation of PKA substrates and decreased induction of $\beta 2$ -AR-responsive genes, while other responses appear normal. Our data suggest the muscle clock regulates aspects of 24-hr hormone sensitivity, and disruption of the muscle clock causes a condition of partial "catecholamine resistance" characterized by decreased muscle response to β -adrenergic agonists.

Key words: circadian rhythms; skeletal muscle; $\beta 2$ -adrenergic receptors ($\beta 2$ -AR); catecholamine resistance. References

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2024Pdm3 February 28 - Abstract 28

Contractile activity and mitochondrial transplantation rescue lysosomal and mitochondrial homeostasis in muscle cells

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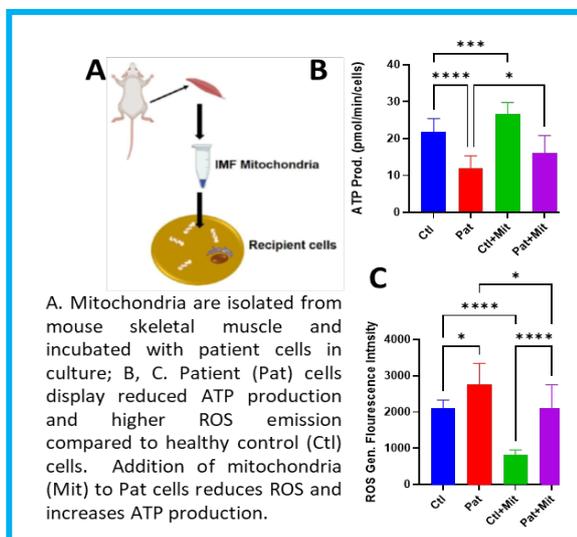
Aging muscle displays a reduction in mitochondrial content, along with elevated reactive oxygen species (ROS) emission, reduced levels of antioxidant enzymes and dysfunctional lysosomes.¹ These characteristics enhance tissue susceptibility to deterioration, facilitating sub-optimal cellular metabolism and subsequent muscle atrophy. While these perturbations to metabolic homeostasis are a natural course of the aging process, there has been ongoing research investigating how to implement interventions to reduce this decline in muscle health. Regular exercise is one possible treatment modality, however this may be unsuitable for some populations who are unable to participate due to their health status. The objective of our recent work is to use a

cell culture model of fibroblasts,² and skeletal muscle cells (myoblasts and myotubes) to identify alternative or adjunct treatments, which could be implemented alongside exercise to improve muscle cell metabolic health. Our myotube model can be subject to contractile activity,³ transfected with expression vector constructs, treated with promising drugs or administered exogenously-derived mitochondria. Recent research that has gained considerable attention is the ability of mitochondria to transfer between cells. This has the potential of improving cellular functions in pathological or energy deficit conditions, but little is known about the role of mitochondrial transfer in sustaining cellular homeostasis. We isolated mitochondria from murine skeletal muscle and incubated them with host cells (4). Dose- and time-dependent increases in mitochondrial incorporation into myoblasts were observed, resulting in elongated mitochondrial networks and an enhancement of bioenergetic profile of the host cells. Mitochondrial donation also rejuvenated the functional capacities of the myoblasts when respiration efficiency and lysosomal function were inhibited by complex I inhibitor rotenone and bafilomycin A, respectively. Murine muscle mitochondria were also effectively transferred to human fibroblast cells having mitochondrial DNA mutations, resulting in augmented mitochondrial dynamics and metabolic functions. This improved cell function by diminishing ROS emission in the diseased cells. Our findings suggest that mitochondria from donor skeletal muscle can be integrated in both healthy and functionally compromised host cells leading to mitochondrial structural refinement and respiratory enhancement. This mitochondrial trafficking and bioenergetic reprogramming to maintain and revitalise tissue homeostasis could be a useful therapeutic strategy in treating disease, or aging muscle.

Key Words: mitochondria; muscle; fibroblasts; exercise; contractile activity; aging.

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Role of mitochondrial permeability transition in driving skeletal muscle pathology in aging and disease

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 February 28 - Abstract 30

Exercise rescues the negative effects of head-down tilt bed rest on muscle and mitochondrial health in older adults.

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Muscle disuse encountered during bed rest, immobilization, and microgravity results in rapid loss of muscle mass and strength, particularly in older adults. Impairments in multiple aspects of mitochondrial function are believed to contribute to disuse- and aging-induced muscle atrophy and weakness (1,2,3). While exercise is well known for its positive impacts on muscle and mitochondrial health (4,5), whether it can protect against the negative impacts of disuse in older adults remains largely unexplored. In this setting, we

investigated the impact of two weeks of head-down tilt bed rest (HDTBR) with and without an exercise countermeasure in older men and women (age range: 55 to 65 years old). Magnetic resonance imaging was used to assess muscle volume. Bergström needle biopsies from the Vastus Lateralis were collected to assess markers of mitochondrial content, respiration, reactive oxygen species (ROS) production and calcium retention capacity. Proteins regulating mitochondrial quality control processes, including markers of fusion (MFN1&2), fission (Drp1) and mitophagy (Parkin), and markers of autophagy (p62 and LC3I&II), were quantified using immunoblots. The proportion of NCAM positive fibers was assessed as a marker of denervation. Head-down tilt bed rest resulted in skeletal muscle atrophy, reduced mitochondrial content and respiration and increased mitochondrial ROS production. Head-down tilt bed rest did not alter mitochondrial calcium retention capacity or mitochondrial quality control markers but resulted in an accumulation of markers of autophagy and an increase in markers of denervation. Exercise protected against the deleterious effects of head-down tilt bed rest on muscle volume, mitochondrial ROS production and markers of autophagy and denervation. Exercise also resulted in an increase in mitochondrial content and respiration, without impacting mitochondrial calcium retention capacity and mitochondrial quality control markers. Taken altogether, our results indicate that an exercise countermeasure that can be performed in bed is effective in protecting muscle and mitochondrial health during of head-down tilt bed rest in older men and women.

Key Words: disuse; skeletal muscle atrophy; mitochondria; autophagy; neuromuscular junctions.

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Mitochondrial stress response in muscular dystrophy and cancer cachexia

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 Febbraio 28 - Abstract 32

The role of the Mitochondrial Calcium Uniporter in Skeletal muscle

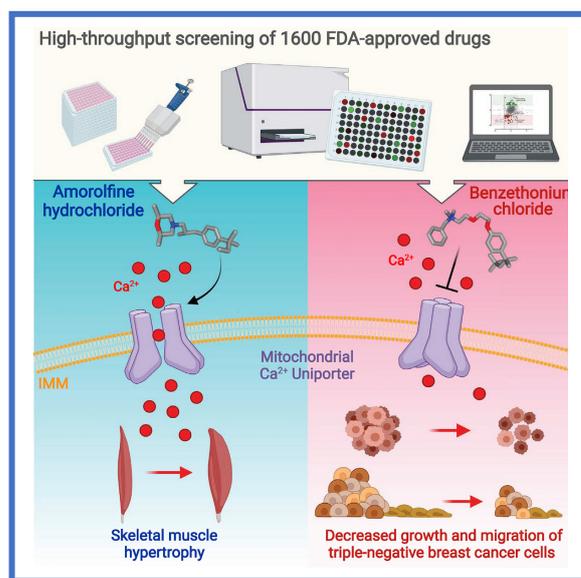
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The skeletal muscle rapidly responds to metabolic challenges including exercise and nutrient availability. In skeletal muscle Ca^{2+} directly contributes to excitation-contraction coupling and to the stimulation of mitochondrial energy production. Mitochondrial Ca^{2+} (mitCa^{2+}) influx serves as a rapid signal for the allosteric activation of specific matrix dehydrogenases of the TCA cycle, and of the mitochondrial ATP synthase. mitCa^{2+} uptake is mediated by a highly Ca^{2+} selective channel, the mitochondrial Ca^{2+} uniporter (MCU). In skeletal muscle, MCU regulates myofiber size by impinging on $\text{PGC1}\alpha$ 4 and IGF1-AKT/PKB pathways (1). Disuse atrophy is associated with changes in mitochondrial morphology, increased mitochondrial reactive oxygen species production and impaired mitochondrial function. While the genetic modulation of MCU has been widely applied, small molecules able to increase mitCa^{2+} uptake are rare. By using a well-established methodology based on Aequorin, a Ca^{2+} -sensitive probe that emits light upon Ca^{2+} binding, we screened a library of 1,600 FDA-approved drugs for their ability to modulate mitCa^{2+} uptake. We identified Amorphine as a positive MCU modulator. Amorphine increases mitCa^{2+} uptake in HeLa, C2C12 cells and adult isolated myofibers without affecting cytosolic Ca^{2+} transients and mitochondrial membrane potential (2). Amorphine induces in vivo skeletal muscle hypertrophy and promotes Akt phosphorylation. It also downregulates the transcription of atrogenes and autophagy-related genes. Moreover, Amorphine protects against denervation-induced muscle atrophy by downregulating ubiquitin ligases



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transcription. Thus, the positive modulation of MCU could represent a novel target in disuse atrophy.

Key words: skeletal muscle; Amorolfine, disuse, mitochondrial calcium.

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2024Pdm3 February 28 - Abstract 33

The energetic expense of inflammation: implications for muscle health

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 February 28 - Abstract 34

Oculopharyngeal Muscular Dystrophy (OPMD) and muscle ageing

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 February 29 - Abstract 35

Simulating weightlessness with inactivity models on Earth: research experience of the Bedrest Centre in Koper

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2024Pdm3 February 29 - Abstract 36

Neuromuscular impairment with chronic inactivity

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 February 29 - Abstract 37

Mononuclear resident cells and skeletal muscle homeostasis in disuse: an overview

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2024Pdm3 Febbraio 29 - Abstract 38

Skeletal muscle oxidative metabolism following disuse/microgravity: where are the bottlenecks?

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Bed rest studies offer a unique opportunity to evaluate the effects of prolonged muscle disuse and unloading, conditions experienced by bedridden patients with injuries and chronic diseases or by astronauts exposed to microgravity during spaceflight missions. Exposure to microgravity/disuse leads to impairment of oxidative metabolism, the main energy source for exercise or work activities lasting longer than 1–2 min. The impairment of oxidative metabolism during exercise is usually identified and quantified in terms of decreases in maximal or “peak” O₂ consumption. However, the sites or functions responsible for this impairment are still debated. Whereas cardiovascular impairments, mainly represented by a decreased peak cardiac output, have been well described, also by our group (Baldassarre et al. 2022), peripheral (microvascular and mitochondrial) impairments appear to be more complex and somehow less defined. According to recent studies by our group (Zuccarelli et al. 2021, Baldassarre et al. 2022)^{1,2} following a relatively short (10 days) period of horizontal bed rest, in young healthy males the main peripheral limitations to oxidative metabolism are “upstream” of mitochondrial function, i.e. at the level of microvascular O₂ delivery. Substantial impairments were indeed observed for biomarkers of microvascular/endothelial function, which is nowadays considered to be crucial in the pathogenesis of many diseases, such as the COVID-19 infection, cardiovascular and metabolic diseases and others. These biomarkers were obtained by determining, by Echo-Doppler, the blood flow increase in the common femoral artery during passive leg movements of one limb (Zuccarelli et al. 2021).¹ Evidence suggesting a transiently (at the onset of exercise) impaired intramuscular matching between O₂ delivery and O₂ uptake was also observed (Zuccarelli et al. 2021).¹ This matching, in which a crucial role is played by nitric oxide availability, is also of critical importance, considering the gross anatomical and functional disparities between neuromuscular and microvascular “units”. A transient

intramuscular mismatch between O₂ delivery and O₂ uptake was observed by our group also following bed rest exposures of longer duration, such as 21 (Salvadeo et al. 2018)³ or 35 days (Porcelli et al. 2010).⁴

On the other hand, following a 10-day bed rest mitochondrial content and maximal ADP-stimulated mitochondrial respiration, determined ex vivo by high-resolution respirometry of permeabilized vastus lateralis muscle fibers obtained by biopsy, were unaffected (Zuccarelli et al. 2021).¹ Evidence of improvements of mitochondrial function (such as an enhanced mitochondrial sensitivity to submaximal [ADP]) was described. An unchanged function of skeletal muscle oxidative metabolism was also confirmed by a biomarker obtained in vivo (muscle O₂ uptake recovery kinetics, determined by near-infrared spectroscopy and the “repeated occlusions” method [Zuccarelli et al. 2021]).¹

At least in functional terms, therefore, mitochondria seem to be relatively resilient to the negative consequences of short-term microgravity/disuse. “Functional terms” is specified in the previous sentence since, according to data obtained by other groups in the same bed rest campaign, a substantial impairment of the “transcriptome” of mitochondrial genes occurs as early as after 5 days of bed rest. In other terms, changes at the level of the transcriptome may become evident before functional changes are observed. The scenario could be different following a more prolonged exposure to simulated microgravity (21 days), a condition in which both respirometric (Salvadeo et al. 2018)³ and proteomic data suggest altered mitochondrial function and structure.

Functional data dealing with longer exposures to microgravity/disuse, dealing specifically with females, older subjects, as well as data specifically investigating the interindividual variability of the responses (ideally allowing to identify biomarkers of individuals less susceptible to the impairments) should represent the objective of future studies.

Key words: microgravity; disuse; skeletal muscle oxidative metabolism; mitochondrial respiration, microvascular/endothelial function.

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2024Pdm3 February 29 - Abstract 39

Muscle sparing effect of high-protein diet with excess leucine in short-term bed rest

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Presentation on site. The author has asked to postpone the submission of the abstract.

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Physical activity and mitochondria. Challenging the paradigm

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We applied mass spectrometry-based proteomics to the analysis of muscle biopsies of two astronauts who spent six months on the International Space Station and had very different levels of physical activity while on board. The two astronauts lost over 20% of fiber cross-sectional area during the mission and displayed consistent loss of strength after landing, despite onboard physical activity. We asked whether, the absence of gravity and weight-load in space causes the same remodeling as inactivity on Earth in skeletal muscle. We thus analyzed in parallel by mass spectrometry-based proteomics the skeletal muscle of ten healthy volunteers who spent 10 full days in bed, developing significant muscle atrophy. We added mechanistic detail by performing single fiber proteomics, to obtain a fiber type-resolved analysis of the effects of inactivity. Our analysis quantified over 70% of all proteins annotated to the mitochondrion. The two atrophy-inducing conditions, spaceflight and bed rest had distinct effects on the mitochondrial proteome, which I will detail in my presentation.

Keywords: proteomics; muscle fibers; mitochondria; astronauts.

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2. Protein profile of fiber types in human skeletal muscle: a single-fiber proteomics study. Murgia M, Nogara L, Baraldo M, Reggiani C, Mann M, Schiaffino S. *Skelet Muscle*. 2021
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2024Pdm3 Febbraio 29 - Abstract 41

Sensitivity of mitochondrial respiration to submaximal [ADP] after bed rest: a new approach based upon different mitochondrial populations.

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We recently demonstrated that a 10-day exposure to inactivity/microgravity (bed rest, BR) determined impairments of peak oxygen uptake and microvascular/endothelial functions,^{1,2} whereas maximal ADP-stimulated mitochondrial respiration (JO₂max) ex vivo was unaffected.¹ Aim of the study was to evaluate mitochondrial sensitivity to submaximal [ADP] by a new approach aimed at identifying different mitochondrial populations. Isolated permeabilized vastus lateralis fibers were analyzed by high-resolution respirometry in 9 young males before and after a 10-day BR.³ We applied to JO₂ vs. [ADP] a traditional Michaelis-Menten kinetics equation, and calculated the apparent Km and maximal respiration (V_{max}), and two “sequential” hyperbolic equations, yielding two Km and V_{max} values. Isoform expression of myosin heavy chains (MyHC) 1, 2A and 2X was determined. The two hyperbolic equations improved the fitting and identified two distinct phases of JO₂ vs. [ADP]: a first phase with low V_{max} (28±10 pmol/s/mg) and apparent Km (62±54 μM), and a second

characteristics analyses suggest that the two mitochondrial populations, responsible for the two phases of JO₂ vs. [ADP], were related to the % of MyHC isoforms.

Funding: ASI, MARS-PRE Project, PRIN n. DC-VUM-2017-006

Key words: bed rest; mitochondrial respiration; ADP-sensitivity.

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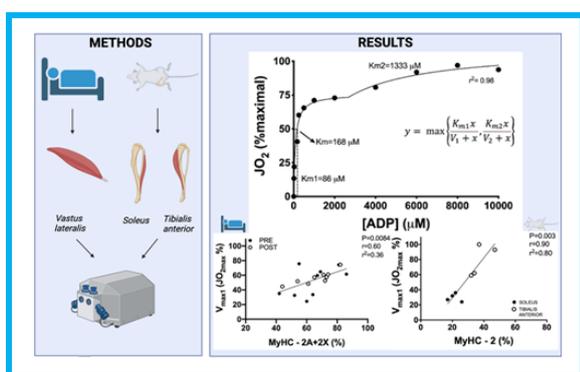
Mitochondrial and Neuromuscular Junction Alterations with Chronic Inactivity in Humans

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Inactivity leads to significant alterations in both mitochondrial function and the stability of the neuromuscular junction (the NMJ). Studies emphasize the adverse effects of disuse on mitochondrial electron transport chain capacity and mitochondrial dynamics,

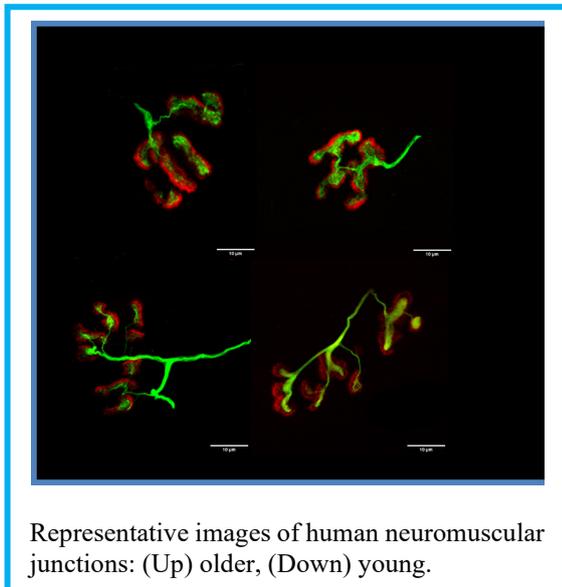


phase with high V_{max} (61±16 pmol/s/mg) and Km (1784±833 μM). [ADP] at 50% JO₂max showed a trend to decrease after BR, suggesting a greater sensitivity of mitochondrial respiration to submaximal [ADP]. Data were confirmed in control experiments carried out in rat muscle samples with different percentages of MyHC isoforms. Correlation and receiver operating

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contributing to impaired energy production and cellular homeostasis in skeletal muscle (Hyatt et al., 2019). Concurrently, research underscores the vulnerability of the NMJ to inactivity, leading to instability and potential dysfunction in motor neuron-muscle fiber communication (Sarto et al., 2022). It has been shown



Representative images of human neuromuscular junctions: (Up) older, (Down) young.

that just 3-days of dry immersion provoke reduction in ADP-stimulated mitochondrial respiration (Popov et al., 2023) and induce early denervation (Demangel et al., 2017). The following study was dedicated to investigating the causes of mitochondrial functional impairment in chronic inactivity by analyzing mitochondrial respiratory complexes and supercomplexes, along with mitochondrial dynamics. Another focus of our study was the assessment of morphological alterations of human NMJ with chronic inactivity. For this, 9 young participants and 10 older participants underwent 21-day and 10-day bedrest, respectively, with a vastus lateralis muscle biopsy obtained before and after the bedrest period. Analyses of mitochondrial respiratory complexes and supercomplexes formation by Blue native PAGE, and mitochondrial oxidative phosphorylation and fission/fusion protein content by SDS-PAGE are currently in progress, along with the ongoing analysis of NMJ morphological alterations by immunohistochemical staining. Seven samples from older individuals tested positive for the presence of NMJs before bedrest, and nine samples tested positive after the bedrest period, with six samples coinciding both before and after. The results obtained will help to unravel the mechanism underlying the impairment of the neuromuscular system induced by chronic inactivity in humans.

Key words: inactivity; mitochondria; electron transport chain; neuromuscular junctions.

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Motor unit properties alterations with chronic inactivity in young and older humans

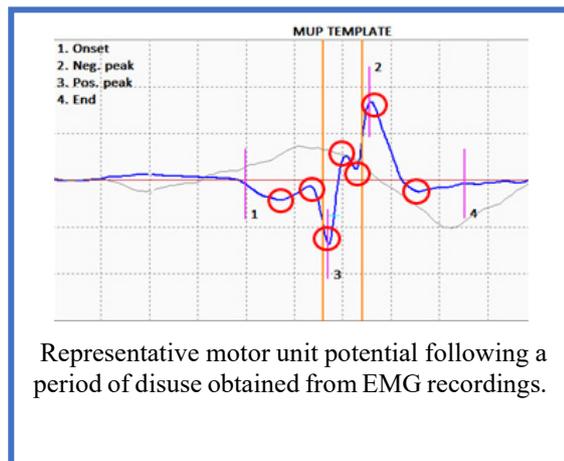
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Periods of disuse lead to rapid and marked decreases in muscle mass and force.¹ Interestingly, the reported loss

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of muscle force largely exceeds that of muscle size, suggesting an impairment in the intrinsic capacity of force production.² Although a clear and exhaustive explanation of this phenomenon is still lacking, there is growing evidence that neuromuscular impairment is a key player in this scenario.^{3,4} In this lecture, observations from intramuscular electromyography (iEMG) recordings providing new insights into the mechanisms of the neuromuscular alterations induced by different disuse models shall be presented.⁵ The findings that will be presented strongly suggest that even brief periods of disuse induce alterations in motor unit properties, such as increased motor unit potential complexity and decreased motoneuron firing rate. The differential adaptations of young and older adults in response to muscle disuse shall also be discussed.

Key words: muscle weakness; electromyography; motor unit; neuromuscular junction; myofibre denervation.

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2024Pdm3 February 29 - Abstract 44

Sensorimotor adaptations during bed rest: insights from high-density electroencephalography

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 February 29 - Abstract 45

Effect of prolonged bed rest on brain functional connectivity measured with high-density electroencephalography

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The relevance of Tensiomyographic results in disuse studies

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Tensiomyographic (TMG) delay, contraction and half-relaxation time correlate with the proportion of myosin heavy chain I proportion,¹ and TMG amplitude correlates with muscle atrophy after disuse.² Moreover, the increase in TMG amplitude precedes a decrease in muscle diameter,³ which is of great clinical importance for older adults undergoing periods of disuse, as they have difficulty recovering afterwards.⁴ Although a clear and exhaustive explanation of TMG changes after disuse is still pending, there is evidence that TMG amplitude increases in all muscles studied after bed rest, with no change in contraction time for the postural muscles, while the contraction time of the non-postural biceps femoris is prolonged.^{2,3} We will compare the changes in skeletal muscle's TMG-derived contractile properties alterations after bed rest and dry immersion studies. In addition, we will show different changes in younger and older men in bed rest studies, while we will show different changes in men and women in dry immersion studies. It appears that age and type of disuses affect TMG-derived skeletal muscle contractile parameters differently.

Key words: Skeletal muscle; Atrophy; Tensiomyography, Bed rest; Dry immersion

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Previous muscle disuse influences the physiological adaptations to exercise recovery

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 February 29 - Abstract 48

Effects of disuse and retraining on oxygen diffusion and oxidative capacity at skeletal muscle level

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Neuromodulatory contribution to lower limb muscle force production after short-term unloading and active recovery

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aspects of well-being among sedentary elderly individuals. In particular, it demonstrates a significant improvement in pain perception and quality of life. By alleviating pain and enhancing overall quality of life, these programs have the potential to promote not only physical, but also mental health, thereby supporting a more independent lifestyle in the elderly population.

Key words: rehabilitation; elderly; physical exercise; sarcopenia.

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2024Pdm3 February 29 - Abstract 53

Cardiorespiratory and neuromuscular adaptations induced by strength training and low-volume, high-intensity aerobic training in untrained young people

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 February 29 - Abstract 54

Effects of high intensity vs. continuous interval training on cardiac autonomic modulation of hypertensive women

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 February 29 - Abstract 55

beta-endorphin levels following acute physical exercise in young and middle-aged adults

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A large and growing body of literature has explored the impact of physical exercise (PE) on human health, shedding light on its crucial role for brain health.¹ Recent research suggests beta-endorphin (β E) as a promising candidate for mediating the exercise-induced stimulation of neurogenesis.² Moreover, PE can elevate the levels of brain-derived neurotrophic factor (BDNF), further promoting the process of neurogenesis.³ To date, few studies have analysed age-related differences in β E secretion following acute PE and no study has investigated its association with BDNF in humans. The purposes of this study were to examine the exercise-induced changes in β E release in two age groups of healthy adult males and to explore potential correlations between β E and BDNF. Thirty-four participants (22 young adults, YA: age, 24.6 \pm 3.5 yrs; BMI, 23.2 \pm 2.3 kg/m²; peak oxygen uptake ($\dot{V}O_{2peak}$), 49 \pm 9.8 ml/kg/min and 12 middle-aged adults, MA: age, 54.6 \pm 5.7 yrs; BMI, 23.4 \pm 2.2 kg/m²; $\dot{V}O_{2peak}$, 44.8 \pm 5.1 l/kg/min), underwent an incremental cycling test to exhaustion. Respiratory gases were measured breath-by-breath using a metabolic cart and venous blood samples were collected before the exercise, 15 min, and 24 h post-exercise. Serum levels of β E and BDNF were measured using ELISA kits. Data were analysed with the Mann-Whitney test, Wilcoxon signed-rank test, and Spearman's correlation. β E levels exhibited a significant increase from baseline (YA: 176 \pm 21.2 pg/ml; MA: 152.1 \pm 21 pg/ml) to 15 post-exercise (YA: 211.7 \pm 30.8 pg/ml, p <0.001; MA: 187.2 \pm 33.5 pg/ml, p <0.01), followed by a significant decline from 15 min to 24 h post-exercise (YA: 180.2 \pm 23.7 pg/ml, p <0.001; MA: 155.7 \pm 23 pg/ml, p <0.01). β E concentration before and at 24 h post-exercise was higher in YA than MA (p <0.01 and p <0.05, respectively). However, no significant differences between groups were found at 15 min post-exercise. For all time points evaluated, no correlation was observed between serum β E and BDNF levels (p >0.05). Serum BDNF levels have been previously reported. Despite the impact of chronological ageing on circulating β E levels, our findings demonstrate that acute PE can induce an immediate increase in β E levels in both YA and MA. The lack of correlation between β E and BDNF suggests that these two molecules might independently contribute to the neurogenic effects of PE on the human brain.

Key words: beta-endorphin; BDNF; acute physical exercise; serum; neurogenesis.

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Brain-Derived Neurotrophic Factor Production in Response to Strenuous Incremental Exercise across Adulthood.

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Brain-derived Neurotrophic Factor (BDNF) is a neurotrophin that plays a pivotal role in memory, learning, and neural plasticity. Its levels can be significantly influenced by various external factors, including physical exercise¹. Many studies have investigated the impact of exercise on BDNF production, in both healthy individuals and various medical conditions²⁻⁵. This study sought to shed light on the temporal dynamics of BDNF production in response to incremental exercise, in particular exploring whether age can influence its release. We enrolled 20 young adults (YA: 24.7 \pm 3.6 yrs.; percentage of fat mass (%FM): 11.1 \pm 5.4 %; peak oxygen uptake ($\dot{V}O_{2peak}$): 49.7 \pm 9.9 ml/kg/min) and 12 middle-aged adults (MA: 54.6 \pm 5.7 yrs.; %FM: 16.7 \pm 6.5 %; $\dot{V}O_{2peak}$: 44.8 \pm 5.1 ml/kg/min). Participants underwent a cycling ramp $\dot{V}O_{2max}$ test until volitional exhaustion. Throughout the exercise regimen, gas exchange was continuously recorded using a metabolic cart. Venous blood samples were collected at three-time points: baseline (T0), 15 minutes after exercise (T1), and 24 hours post-exercise (T2). Serum BDNF (sBDNF) levels were quantified using an ELISA

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kit. Statistical analyses were performed with SPSS (ver. 27). Wilcoxon signed-rank test was employed to analyse the differences in sBDNF concentration throughout time points. Mann-Whitney U test was used to analyse differences in sBDNF concentration between groups. Results were considered significant when $p < 0.05$. Surprisingly, we did not observe significant changes in sBDNF levels from T0 to T1 for both the YA and MA groups. However, a remarkable increase in sBDNF was detected from T0 (YA: 13.3 ± 1.69 ng/ml and MA: 12.7 ± 0.9 ng/ml) to T2 for both groups (YA: 15.5 ± 3.5 ng/ml, $p < 0.001$; MA: 14.4 ± 3 ng/ml; $p < 0.05$). Importantly, there were no statistical differences in sBDNF levels between age groups at any of the time points. This study provides new insights into the age-related effects on sBDNF release following acute strenuous exercise within a substantial cohort of healthy adult males. Contrary to previous findings, our results exhibit that acute exercise can stimulate delayed sBDNF release, irrespective of age, 24h post strenuous exercise. These results emphasize the critical role of physical exercise in promoting neurogenesis and neural plasticity throughout the entire lifespan. Given the importance of exercise induced BDNF release in enhancing cognitive functions, such as memory and spatial learning, regular physical exercise should be included into daily routines, even for middle-aged and older individuals.

Key words: BDNF; Acute Physical Exercise; Aging.

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The impact of the isocapnic hyperpnea respiratory muscle training on diaphragm structure and function

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Presentation on site. The author has asked to postpone the submission of the abstract.

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Etiology, Identification and Treatment of Chronic Muscle Spasm and Resultant Chronic Pain with the CMECD® Procedure

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One of the most frequent causes of chronic pain is acquired chronic muscle spasm. This is to be distinguished from chronic muscle spasm of a neurologic etiology such as found in post stroke patients. Acquired chronic muscle spasm has a distinctive EMG presentation with chaotic and high grade spontaneous electrical activity known as SEA. What has not been appreciated is that the SEA is not only a characteristic finding of chronic muscle spasm but also the responsible agent. Elimination of the SEA results in resolution of the muscle spasm. Temporary resolution of SEA with a short acting agent such as Lidocaine will give relief by a combination of its anesthetic and antiarrhythmic properties. But it is the antiarrhythmic property that is responsible for at least temporary relief of muscle spasm that is likely to return when the SEA suppression wears off. I found that a longer acting agent, such as phenoxybenzamine, used in combination with Lidocaine can maintain suppression of the SEA and result is resolution of the chronic muscle spasm and its resulting chronic pain. The spocedure I developed is trademarked

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under the name CMECD® which is an acronym for Coletti Method Emg guided ChemoDenervation. With this procedure, chronic muscle spasm even if present for decades can be resolved without recurrence by a single treatment. Moreover, recovery from the damaging effects of chronic muscle spasm that include loss of mitochondria and muscle fiber can occur gradually over time. In the current formulation, the injectate includes Lidocaine, phenoxylbenzamine and dexamethasone. EMG guidance is critical to the procedure as the initial effect of the injectate is that of Lidocaine with clear and obvious suppression of the SEA. The effect of phenoxylbenzamine takes effect within one hour to maintain the SEA suppression for a prolonged period. The mechanism of action is the formation of a covalent bond on the alpha adrenergic receptor. The clinical duration of action is two to three months as the muscle tissue replaces the nonfunctional receptors. The dexamethasone was added to the injectate to minimize the inflammatory response to the phenoxylbenzamine which unfortunately is a tissue irritant. Typically, the inflammatory reaction resolves in three to four days and is seldom severe. What must be kept in mind is that muscle that has been in chronic spasm is damaged and even with rapid resolution of the spasm, cannot be expected to function at pre spasm work loads without recreating an overuse injury that had been responsible for the chronic muscle spasm in the first place. This is in part due to the loss of mitochondria and muscle fibers. These findings were documented by the work of Ugo Carraro which I characterized as Hibernating Skeletal Muscle comparing it to Hibernating Myocardium known to the cardiology world. The etiology of Hibernating Myocardium is ischemia caused by narrowed or blocked coronary arteries. In the case of Hibernating Skeletal Muscle, I have proposed that ischemia is present and responsible for the tissue damage. I have proposed that the ischemia is secondary to prolonged untreated muscle spasm limiting its own vascular supply. I have proposed the Ischemic Model of Chronic Muscle Spasm. Support for this concept comes in part from basic animal research I performed during my cardiology fellowship which I neglected to publish at the time not realizing its significance. My findings were that progressive suppression of myocardial contraction would lead to a reversal of the flow dynamics of coronary blood flow such that predominant flow would be in systole. It has been well documented that coronary blood flow is predominant in diastole when the coronary artery capillaries are not being compressed by myocardial contraction. As another corollary to cardiac pathophysiology, ischemic cardiac muscle is prone to arrhythmias. In the most simplest sense, the SEA that is the driving force for the persistence of muscle spasm, is simply a skeletal muscle arrhythmia from self induced ischemia. With the presented encompassing picture of chronic muscle spasm pathophysiology, it should be

possible to further extend treatment options that in addition to the CMECD® procedure can relieve chronic pain secondary to chronic muscle spasm without the use of opioid medications.

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Key words: chronic muscle spasm; chronic pain; EMG guided chemodenervation; CMECD; phenoxylbenzamine.

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Predicting Development of Chronic Musculoskeletal Pain

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Musculoskeletal pain is the most frequent pain problem among the adult population but 1) fundamental knowledge of underlying mechanisms for chronification and 2) adequate options for long-term treatment options are still lacking. The pain intensity experienced by patients with chronic musculoskeletal pain has often no relation to the actual insult or size of damage e.g. minimal joint damage may cause severe pain whereas severe joint degeneration may cause minimal pain. A variety of factors may explain this disconnects including eg. psychological factors, sleep quality, pain amplifications in the peripheral and central nervous systems, genetic factors, and most recently epigenetic factors. Few longitudinal clinical studies have been performed to understand factors contributing to the development of a future de novo painful musculoskeletal condition. Most studies have been focused on predicting musculoskeletal pain after e.g. a traumatic event (accidents or surgery). Recently, the COVID-19 pandemic provided an opportunity for large sample studies as patients were infected with fundamentally the same virus and some may develop long-COVID musculoskeletal pain whereas others do not. Recent advances in AI and processing of large datasets for predicting outcome is now an option and an example will be given on using AI for analysing large datasets to predict development of musculoskeletal pain. As long-term pharmacological management of chronic musculoskeletal pain is generally not an option and other non-pharmacological/conservative treatment procedure such as training are needed but few systematic, randomized, controlled studies have been performed to understand which training features are the most important to apply in a multidisciplinary pain management program. The lecture will provide an update on the most recent predictive factors for development and maintaining painful, chronic musculoskeletal conditions and future ideas/options for safe and efficient management.

Key Words: development; chronic pain; musculoskeletal pain; prediction; biomarkers.

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Transformative care for myopain: Integrating training with treatment to improve long-Term outcomes

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Presentation on site. The author has asked to postpone the submission of the abstract.

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The role of external-focus exercise & exergaming in pain management

Jan Dommerholt

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Compliance with therapeutic exercise programs is generally poor, with over 70% of (low back) patients failing to perform their prescribed exercises. One of the many reasons for this poor compliance may be the frequent use of an internal focus exercise approach, which is often experienced as boring, repetitive, pointless, and non-productive. This lecture will challenge current belief systems about exercise and the way you practice and prescribe therapeutic exercise. This brief session integrates contemporary research, including the OPTIMAL Theory of Motor Learning, exergaming technology, and pain science into a new therapeutic conditioning and exercise method using primarily an external-focus approach. Compared to internal focus exercise programs, directed at the performer's own body movements, external focus programs, directed at the effects of movement on the environment, have immediate beneficial effects on performance, retention, and transfer. Improvements are observed in movement effectiveness and efficiency, self-efficacy, confidence, automaticity of control, and overall cognitive function.

Key Words: external-focus exercise; exergaming; pain.

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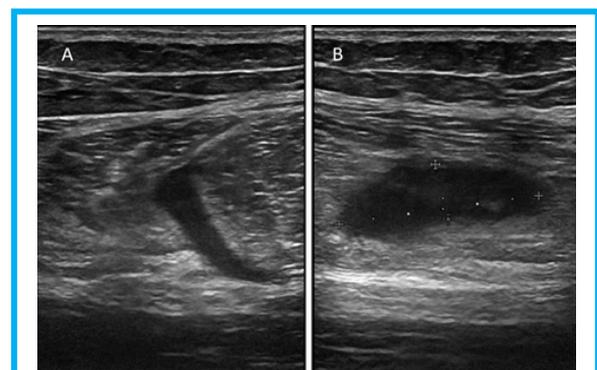
Anti-pain rehabilitation management of muscle injuries

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Muscle injuries are very common in sports, particularly in professional and amateur soccer players, with an incidence of about 8.1 injuries per 1000 hours of exposure. The injury rate obtained for the matches is notably higher (almost 10 times) than the injury rate during the training sessions.¹ 92% of muscle injuries

affect the lower extremities, with a higher prevalence in the thigh, especially in the hamstring muscles. Lower limb muscles injuries are also frequently found in track and field athletes (16%), rugby (10.4%), basketball (17.7%), American football (22%) and tennis.¹ Eccentric contraction represents both an injury mechanism in the suffering muscle and a preventive strategy in the healthy muscle. Indeed, the force expressed by the muscle with eccentric-type exercise is 30-40% higher than with a concentric-type exercise.² Patient's assessment requires the collection of a careful medical history, an objective examination, and the appropriate instrumental evaluation (ultrasonography and/or Magnetic Resonance Imaging - MRI), to be performed at least 48 h after the acute event, to better define and quantify the severity of the muscle damage. A proper rehabilitation treatment requires the knowledge of the reparative processes and the biological timing of injury healing. Indeed, skeletal muscle has the capacity to regenerate and remodel after injury thanks to a stem cells population, also known as satellite cells (SC). SC, with other functional cell types, act as myoblasts, that, when properly stimulated, allow regeneration of damaged tissue.³ Acute phase treatment focuses on pain and swelling control, requiring the application of the P.O.L.I.C.E. (Protection, Optimal Loading, Ice, Compression, Elevation) protocol, both with the aid of short-term use of NSAIDs (nonsteroidal anti-inflammatory drugs) and antalgic physical therapies not involving the use of heat. In this phase, pain is a load capacity reducing factor (inhibiting proper neuromotor activation) but also represents a protective factor, defending tissue repair and healing. Therefore, therapeutic exercises should be performed with respect to the painful symptomatology.⁴ Subsequent phases provide the introduction of exercises to recover involved joint's range of motion, muscle extensibility (equal to at least 90% of the healthy contralateral), with the help of stretching, massage techniques and hydrokinesitherapy.



Ultrasound image of hamstring's muscle injury: the area of lesion appears hypoechoic. **A.** Transverse sonogram. **B.** Longitudinal sonogram.

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Strengthening phase involves the initial introduction of isometric exercises at different joint grades and, at a later stage, the introduction of isotonic exercises, to be performed always under pain threshold and with progressive loads. Finally, eccentric contractions will be introduced, to prepare the muscle again for athletic gesture.⁵ At this stage, therapeutic exercise can be complemented by specific physical (shock waves) and minimally invasive (prolotherapy, Platelet Rich Plasma-PRP) regenerative therapies to reduce the recovery time, accelerate the time to resume daily and sports activities in athletes, but also elderlies.

Key words: muscle injury; muscle pain; eccentric exercise; muscle rehabilitation.

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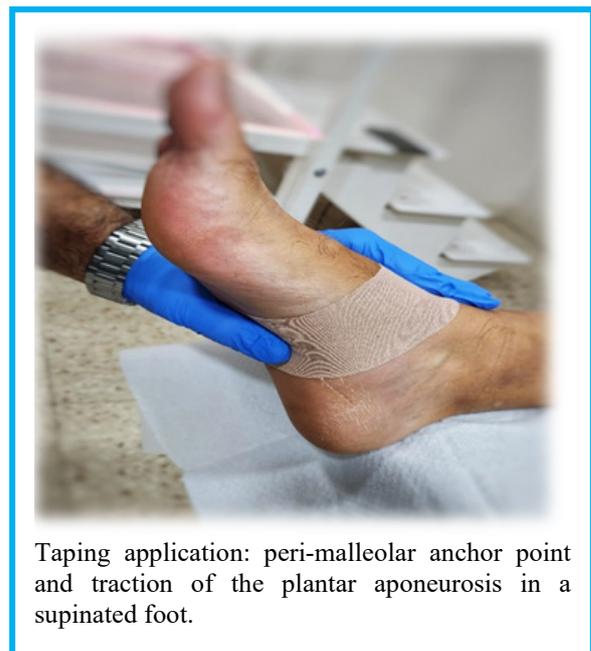
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New frontiers in the treatment of pain in acute plantar fasciitis: Ozoile-soaked taping

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Plantar fasciitis can be described as a calcaneal enthesopathy that causes acute pain especially in the early morning, during early orthostatic phases. Subsequently the pain usually reduces in intensity within 5-10 minutes, and then returns in the course of the day. Plantar fasciitis affects a large part of the world population: not only sedentary people, but also athletes. Among others, obesity, foot pronation, running on hard surfaces, and prolonged standing are risk factors for developing plantar fasciitis. This study looked to the treatment of pain in this pathology using an innovative model approach: an Ozoile-soaked taping. It is a hypoallergenic biodynamic tape with a double



Taping application: peri-malleolar anchor point and traction of the plantar aponeurosis in a supinated foot.

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therapeutic effect equipped with rechargeable microcells indicated for post-operative, traumatic, arthritic, rheumatic, neuropathic pain and myalgia. Ozoile is a pool of molecules produced in a patented process by reaction of a defined oxygen-ozone mixture with the fatty acids of the extra virgin olive oil +OIL® from Erbagil Tenuta. The process leads to the formation of Stable Ozonides. Stable Ozonides have shown documented healing biological activities in addition to an anti-inflammatory and pain-relieving action. The anti-inflammatory properties of ozoile occurs by reducing the levels of pro-inflammatory cytokines such as TNF- α , IL-1 β and IFN- γ and by inhibiting NF-kB with consequential block of the release of inflammatory molecules. A total group of 30 patients was enrolled, divided into two subgroups of 15 individuals, one control group and one study group. The examined patients were aged 35 to 69, BMI 18,5 to 24,9 with a healthy lifestyle and at least 2 hours of motor activity per week, excluding jump sports. Patients were asked to rate their pain on an NRS scale during the first encounter and then re-evaluate it after 15 days and after another 15 days using the same method. During this period, medicated taping was applied to the painful part and therapeutic rest was indicated for the duration of the treatment. Along with the indicated treatment, a cold bag with ice was recommended to be applied for 15 minutes twice a day. The control group followed only a therapeutic rest protocol and the use of a cold bag for 15 minutes a day, twice a day. The study group using the Ozoile molecule in the proposed treatment pathway had a 21.30% $p < 0.004$ improvement from T0 to T1 and 68% improvement from T0 to T2 $p < 0.002$. The control group, on the other hand, had a T0 to T1 improvement of 19% $p < 0.006$ and from T0 to T2 of 40% $p < 0.004$.

Key words: plantar fasciitis; rehabilitation; pain; Ozoile; stable ozonides.

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2024Pdm3 February 29 - Abstract 64

Perspectives of over 20 years of FES to treat equine muscle spasms and the potential crossover into humans

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Presentation on line. The author has asked to postpone the submission of the abstract.

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2024Pdm3 March 1 - Abstract 65

Cellular actors and ECM components of human fibrosis in myopathies

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Fibrosis is defined as the excessive accumulation of extracellular matrix (ECM) components as a result of a failed tissue-repair process. In muscle, fibrosis is one of the main complications in many clinically and pathologically different muscle diseases including Duchenne muscular dystrophy (DMD), oculopharyngeal

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muscular dystrophy (OPMD), inclusion body myositis (IBM) or fascio-scapulothoracic muscular dystrophy (FSHD). Excessive accumulation of ECM alters the muscular function and the potential innovative therapeutic strategies. Several cellular actors are known to be implicated in the establishment and the maintenance of the fibrosis: macrophages, fibroadipogenic progenitors (FAPs) as well as satellite cells. The ECM, apart from its essential role as an architectural scaffold, has also a pivotal role in this process influencing muscle-resident cells through biochemical and biomechanical signals. Today there is no efficient treatment to cure muscle fibrosis, that represents a serious hurdle for the different therapeutic approaches which are now arriving in the clinic. Combining mass cytometry, transcriptome profiling, secretome analysis,¹ in vitro co-culture experiments and in vivo transplantation in immunodeficient mice, we investigated the role and nature of FAPs from human fibrotic muscles and compared them to FAPs from healthy muscle. Our results show that human FAPs from fibrotic muscles display a strikingly different profile than FAPs from non fibrotic muscles with an exacerbated proliferation and ECM secretion, and a detrimental effect on muscle differentiation.² In parallel now, using mass spectrometry, we are characterizing the ECM composition of human skeletal muscle biopsies from several myopathies. We identified a few shared ECM protein components as well as many specific ones for each pathology, highlighting differences in the amount and nature of ECM components. Altogether, this work on human muscle biopsies provides a better understanding (a) of the key role of FAPs and their cross-talk with muscle cells through a paracrine signaling pathway and (b) of the ECM proteome of the muscle in pathological conditions, with the final objective to identify key components and targetable pathways for anti-fibrosis therapies.³

Key words: muscle fibrosis; extracellular matrix; ECM; dystrophies; FAPs.

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Hyaluronan and aging --The Effects of Aging on the Intramuscular Connective Tissue

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Aging increase passive stiffness of skeletal muscles.¹ The intramuscular connective tissue (IMCT) plays a critical role in maintaining the structural integrity of the muscle and in providing mechanical support.² Alternations of extracellular matrix (ECM) of IMCT influence force transmission and passive elasticity of muscle.³ Hyaluronan (HA), an key elements in ECM, is essential for IMCT preserving muscle structure integrity and affecting fascia gliding.⁴ We will describe age related changes that may contribute to passive stiffness and functional impairment of skeletal muscles. Variations in the extracellular matrix in human quadriceps femoris muscles in 10 young men, 12 elderly males and 16 elderly females, and in the hindlimb muscles of 6 week old, 8 month old and 2 year old C57BL/6J male mice, were evaluated. Picrosirius red, Alcian blue and Weigert Van Gieson stainings were performed to evaluate collagen, glycosaminoglycans and elastic fibers. Immunohistochemistry analyses were carried out to assess collagen I, collagen III and hyaluronan. The percentage area of collagen was significantly higher with aging ($p < 0.01$ in humans, $p < 0.001$ in mice), mainly due to an increase in collagen I, with no differences in collagen III ($p > 0.05$). The percentage area of elastic fibers in the perimysium was significantly lower ($p < 0.01$) in elderly men, together with a significant decrease in hyaluronan content both in humans and in mice. No significant differences were detected according to gender. The lower level of HA together with reduction of elastic fibers and accumulation of collagen fibers with aging could cause stiffening of muscles and reduction of their adaptability.

Keywords: aging; muscle; intramuscular connective tissue; extracellular matrix; hyaluronan.

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How denervation influences the fascia? The Impact of Sciatic Nerve Denervation on Hyaluronan in Intramuscular Connective Tissue and Deep Fascia

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Peripheral nerve injury (PNI) is a complex clinical challenge due to its diverse range of symptoms impacting quality of life.¹ Denervation alters extracellular matrix (ECM) in intramuscular connective tissue (IMCT) affecting muscle function.² Hyaluronan (HA) is essential for IMCT preserving muscle structural integrity and affecting fascia gliding.³ Our study evaluated HA concentration in denervated, non-denervated muscles and the thoracolumbar fascia (TLF) in unilateral lower limb PNI rats to explore the broader denervation effects. Eighteen 8-week-old male Sprague-Dawley rats were divided into two groups: experimental (n=12) with left sciatic nerve injury and control (n=6). After six weeks, muscles (gastrocnemius and soleus) and TLF samples were extracted from all the rats. Purple-Jelley HA assay was employed to determine HA concentration; Alcian

blue and Immunohistochemistry were performed to evaluate HA distribution. In unilateral lower limb PNI rats both sides show significantly lower HA concentration than healthy rats (p<0.05), although with no significant difference between the left and right sides (p>0.05) in the muscles. Moreover, PNI rats showed significantly lower HA concentration in both left and right TLF than healthy TLF (p<0.001), with significantly lower HA in left TLF (homolateral) than right TLF (contralateral) (p<0.001). In conclusion, unilateral lower limb PNI induced HA reduction in denervated muscle and non-denervated muscle of the contralateral side and in the TLF, potentially increasing the risk of low back pain.

Keywords: denervation; muscle; intramuscular connective tissue; thoracolumbar fascia; Hyaluronan.

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Ultrasound evaluation of the fascial gliding

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In the field of musculoskeletal imaging, ultrasonography emerges as a potent tool for identifying numerous pathological conditions that impact the myofascial system, encompassing the deep muscular fascia.¹ Due to its cost-effective, real-time, and noninvasive characteristics, ultrasound examination stands as the

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primary choice for diagnosing pathologies based on the fascia.² Several studies have also confirmed the importance of ultrasound examination of the deep/muscular fascia in various pathological conditions.³⁻⁵ Ultrasonography examination assumes a pivotal role in the comprehensive study of fascial anatomy and pathology from a rehabilitative standpoint.³⁻⁵ The versatility of ultrasound enables the visualization of various aspects, including the thickening of specific fascial layers, alterations in their echogenicity, and the intricate analysis of relationships among fasciae, nerves, and vessels.^{1,2} Noteworthy findings from recent studies indicate that ultrasound facilitates an in-depth exploration of the dynamic interactions,⁶⁻⁸ such as gliding movements between muscles and their adjacent fascial layers, as well as those occurring between diverse fascial layers. These dynamic relationships have been suggested to have relevance to the understanding of myofascial pain.

Key words: Ultrasound examination; fascial gliding; deep muscular fascia; myofascial pain; muscle.

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Hyaluronans and glycosylated proteins in mobility disorders: from research to clinical application

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This lecture will focus on hyaluronans (HA) and glycosylated proteins involved in musculoskeletal disorders, and their properties in regenerative medicine. HA are a naturally occurring biopolymers which play essential roles in the organization of tissue architecture and the regulation of cellular functions, such as cell proliferation, wound healing, cell migration, and signaling (Yasin A. et al., 2022).¹ The cluster determinant 44 (CD44) embedded in the cell membrane mediates adhesion, migration and intracellular signaling as well (Ponta H. et al., 2003).² The cell surface microarchitecture resulting from HA and specific receptor interactions provide an interface between the pericellular milieu and the intracellular cytoskeleton/signaling complexes that is particularly sensitive to ROS/RNS levels, which cleave the native HA polymer, modifies CD44 patterning from its homeostatic microarchitecture,

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and initiates signaling pathways contributing to a response-to-injury and disease (Cowman M. K. 2023).³ Moreover, the HA versatility have made it a key player in biomedical research and led to its use in a wide range of applications, including tissue muscle ligament and tendon repair and engineering. In the last decade we have seen the development of HA derivatives with different clinical applications and potential. HA's ability to, directly and indirectly, affect the wound healing process makes it a key component in regenerative medicine. In muscle, for example, recent evidence demonstrates that HA activates stem cells to repair damaged muscle, indeed the regenerative effect of HA seems to depend on it being produced by the muscle stem cells (Nakka et al., 2022).⁴ In a preliminary experiment, we have analyzed the effect of HA blend of 2 to 1000 KDa, 2 mL on the rescue of myoblasts cells C2C12 under stressed conditions in which in muscle cell damage and a subsequent in a chronic inflammatory state, we evaluated the wound healing of myoblast cell monolayer in the presence of HA blend of 2 to 1000 KDa and pro-inflammatory agents (IL-1 β , TNF- α , LPS) and pro-oxidants (H₂O₂) that slow their proliferation. From the preliminary results obtained, it appears that HA possesses significant pro-proliferative activity and improves wound healing in the 24 h after injury (Ferrini F. et al., in preparation).⁵ Furthermore, some recent studies show encouraging results on HA's capacity to induce tendon healing, improve tendon architectural organization and ameliorate pain and damage recovery (Kaux JF et al., 2016).⁶ In this regard, we demonstrated that in the treatment of Achilles tendinopathy (AT) in middle-aged runners combining viscoelastometric, biochemical, and functional methodologies with routine clinical examinations the sequential peritendinous injections of HA were effective in improving clinical symptoms, as well as functional and viscoelastic state associated with AT (Barbieri et al., 2019; Gervasi M. et al., 2021).^{7,8} In addition, exogenous HA can improve chondrocyte HA synthesis, reduce the degradation of cartilage and facilitate its regeneration. It can also control the release of proinflammatory mediators and matrix metalloproteinases involved in osteoarthritis pathogenesis. Nowadays to the well-known functions exerted by extracellular hyaluronan and glycosylated proteins, recent metabolomic approaches have also revealed that its synthesis can regulate cellular functions via the reprogramming of cellular metabolism in mobility disorders. The last decade shed plenty of light with the significant advances in research related to HA and glycosylated proteins in mobility disorders as well as the extracellular matrix interactions networks. Despite the correlation between several matrix macromolecules with musculoskeletal disorder development and progression, this area of interest has been underestimated in terms of designing novel strategies for disease treatment.

Key words: musculoskeletal disorders; hyaluronic acid; CD44; inflammation.

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The interactions between hyaluronic acid and extracellular vesicles in osteoarthritis: new evidence and therapeutic implications

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Osteoarthritis (OA) is the most common joint disease in the adult population worldwide.¹ OA is the result of multiple mechanisms that lead to chronic inflammation and progressive degradation of the extracellular matrix of the joint. A complex series of cellular and soluble actors along with their articulated temporal interplay have been identified so far as prominent etiological factors. More recently increasing attention has been paid by researchers to the role of extracellular vesicles (EVs) in OA, as well as in the maintenance and recovery of joint homeostasis.² EVs, such as exosomes and membranous EVs, are being extensively studied for their role in a vast number of processes, such as intercellular communication and cell-to-cell transfer of biologically active material due to their peculiar capacity to transfer proteins, lipids, DNA, mRNA, miRNA to target cells, modifying their phenotype. Importantly, EVs are also being studied as potential therapeutic agents for musculoskeletal disorders.³ With regard to the joints and OA, the latest scientific evidence indicates that EVs act in a bimodal pattern, i.e. either in a pro-inflammatory or anti-inflammatory fashion depending on the joint conditions and disease status. As a mere example of their “bad guys” side, it is known that in OA the macrophages infiltrated in the synovial fluid release specific EVs containing proinflammatory cytokines such as IL-1 β ; these cytokines stimulate the chondrocytes to release further EVs which in turn increase the levels of metalloproteinase-13 and of disintegrin and metalloproteinase with thrombospondin motif 5 Type 1 (best known with the acronym ADAMTS-5), the main enzymes responsible for cartilage degradation. Hyaluronic acid (HA) is a polysaccharide composed of disaccharide units containing N-acetylglucosamine and

glucuronic acid produced by chondrocytes, synoviocytes and fibroblasts. Native HA is typically released inside the synovial space where it lubricates and cushions the joint. The physiological balance between HA synthesis and degradation, its size, integrity and abundance play a prominent role in determining the joint's fate. Replenishing HA through the intrarticular injection of exogenous > 500 KDa/1 MDa HA, i.e. the so-called viscosupplementation, has established as a first-line conservative treatment of OA, in particular knee arthritis. The benefits of HA viscosupplementation have been traditionally ascribed to its rheological properties, that accomplish and restore joints' physiological requirements when it is in the native, high molecular weight form. However, evidence accumulated over the last decades also indicates that HA exerts pleiotropic activity within the joint, i.e. not limited to the mere rheological function. Indeed, many molecular targets of HA - whose modulation concurs to its therapeutic efficacy have been identified so far.⁴ Although scientifically attractive for the potential pharmacological implications, the possible interactions between HA and EVs in the course of OA have not yet been specifically addressed. Our study has been aimed to investigate whether HA is capable to affect a panel of relevant responses induced by EVs on target primary chondrocytes. Primary chondrocytes (CS) were obtained from surgical specimens of OA patients undergoing knee arthroplasty; EVs were collected from unstimulated or IL-6 (used as an inflammatory trigger) -stimulated THP1 human monocytes; HA was a commercially available preparation of linear (500 KDa) HA and cross-linked (1, 2 MDa) HA routinely used to treat Kellgren II-III knee OA. Experimental setting was based on the exposure of CS to unstimulated (EV-) or IL-1 β -stimulated (EV+) in the absence or presence of HA. Results obtained indicate that unlike EV-, incubation with EV+ elicited detrimental and inflammation-like responses in CS, namely increased levels of IL-6 and of MMP-13, and accumulation of oxidative-stress by-products. Interestingly HA significantly hampered these responses suggesting a modulatory/normalization role for HA toward EV+ signalling. Further experiments aimed at evidentiating the possible interactions between HA and EVs indicated that HA tightly binds to EVs. It is postulated that the binding with HA may affect the level and frequency of interactions of EV with target cells. It can also be inferred that the higher the MW of bound HA the fewer the interactions: to this regard the integrity of joints' HA (very high MW in healthy joints vs low MW during OA) may underlie a biological function not limited to the rheological homeostasis.

On the whole these results pinpoint to a role for HA in modulating the responses elicited by EV which might take place in in vivo conditions; future studies will be

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needed to better understand HA-EV interactions as well as their possible therapeutic exploitation.

Key words: osteoarthritis; hyaluronic acid; extracellular vesicles; inflammation.

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2024Pdm3 March 1 - Abstract 71

Calcium crystal in the synovial fluid and glycosaminoglycan damage in labrum of patients with femoroacetabular impingement: impact in joint mobility

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Over the last decade, evidence has mounted for a prominent etiologic role of femoroacetabular impingement (FAI) in the development of early hip osteoarthritis (HOA). This is the most common joint disorder and a major cause of disability in the adult population.^{1,2} Thus, the early diagnosis, prevention, and treatment of the early stages of the disease and of the pre-arthritis condition, in particular in adolescents and young adults, is crucial to reducing the incidence of end-stage

HOA and the need for total hip replacement (THR). Femoroacetabular impingement (FAI) has an important role in the development of cartilage, synovial and labral damage in the non-dysplastic hip,³ these morphological and functional modifications can be induced by HOA. An impaired lubrication and an increased joint friction deteriorate articular cartilage and lead to present in patients with FAI.⁴ In vitro and preclinical data demonstrate that calcium crystals can activate intra-articular proinflammatory pathways and release nociceptive stimulating substances. Thus, calcium crystal deposition may be involved in generating joint pain and have a powerful impact in decreasing joint mobility. The aim of this study was to compare the ultrastructure of the hip labrum and cartilage in healthy and pathological conditions, as FAI and OA, to provide understanding of structural changes which might be helpful in the future to design targeted therapies and improve treatment indications. We also investigate the potential associations among the preoperative symptoms, the outcomes after arthroscopic surgery for FAI and the presence of crystal deposition in synovial fluids (SFs). Patients scheduled for hip arthroscopy for treatment of FAI and/or labral pathology were enrolled. We analyzed labral tissue and cartilage samples from five healthy multi-organ donors (MCDs) (median age, 38 years), five FAI patients (median age, 37 years) and five late-stage OA patients undergoing total hip replacement (median age, 56 years). We evaluated morpho-functional by histology and transmission electron microscopy. SFs samples, when available, were obtained by aspiration just prior to surgical intervention, collected and stored as intact for microscopic crystals identification by compensated polarized light microscopy and quantitative analysis by alizarin red staining. Energy Dispersive X-ray Analysis (EDX) was also performed for the chemical analysis of SFs. In conclusion, labral tissue of patients with FAI had similar pathological alterations of tissue obtained from OA patients, suggesting that FAI patients might have high susceptibility to develop OA. In addition our study showed that calcium crystals levels in SFs of FAI patients are correlated with worst post-operative outcome, and it might be used as a potential new biomarker for early diagnosis, prognosis and monitoring of therapeutic responses.

Key words: Calcium crystal; synovial fluid; glycosaminoglycan damage; femoroacetabular impingement.

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2024Pdm3 February 29 - Abstract 72

Remodeling of intracellular organelles during exercise: muscle strategies to reduce muscle fatigue

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 February 29 - Abstract 73

The ERG1A K⁺ Channel Lowers Expression of Calsequestrin 1 and Increases Intracellular Calcium in Skeletal Muscle

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Presentation on line. The author has asked to postpone the submission of the abstract.

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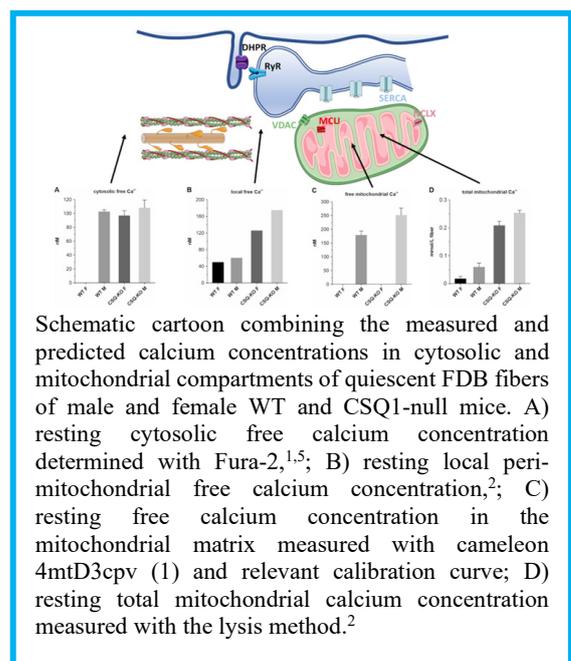
2024Pdm3 March 1 - Abstract 74

A model analysis of cytosolic calcium gradients and mitochondrial Ca²⁺ uptake in resting muscle fibers

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In muscle fibers of transgenic mice model with increased leakage of Calcium ions (Ca²⁺) from sarcoplasmic reticulum (SR), mitochondria display higher mitochondrial calcium concentrations at rest.^{1,2} Since Ca²⁺ enters mitochondria via mitochondrial calcium uniporter (MCU), driven by electrical and concentration gradients, a higher cytosolic calcium concentration is expected as a link between the calcium leakage and the calcium accumulation in mitochondria. We checked this hypothesis in calsequestrin knock-out (CSQ-KO) mice. We determined free Ca²⁺ concentration in SR and mitochondria with specifically targeted cameleon probes and in cytosol with Fura-2. Surprisingly, repeated measurements of cytosolic Ca²⁺ concentration in quiescent CSQ-KO fibers never showed a difference between WT and CSQ-KO.¹ Taking into account that fluorescent Ca²⁺ probes as Fura-2 measure averaged



Schematic cartoon combining the measured and predicted calcium concentrations in cytosolic and mitochondrial compartments of quiescent FDB fibers of male and female WT and CSQ1-null mice. A) resting cytosolic free calcium concentration determined with Fura-2,^{1,5}; B) resting local perimitochondrial free calcium concentration,²; C) resting free calcium concentration in the mitochondrial matrix measured with cameleon 4mtD3cpv (1) and relevant calibration curve; D) resting total mitochondrial calcium concentration measured with the lysis method.²

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global cytosolic concentrations, we explored the role of local Ca^{2+} concentrations (i.e., Ca^{2+} microdomains) in resting cells, using a multicompartamental diffusional Ca^{2+} model.³ Progressively including the inward and outward fluxes of sarcoplasmic reticulum, extracellular space, and mitochondria, we explored their contribution to the local Ca^{2+} distribution within the muscle fibers. The results showed the presence of Ca^{2+} concentration gradients with hot spots or microdomains,⁴ in the region close to the Ca^{2+} release units (CRU) even at rest, minor but similar to those of evoked Ca^{2+} release. Due to their specific localization close to the CRUs, mitochondria are able to take up Ca^{2+} directly from high concentration microdomains. This explains the presence of high mitochondrial Ca^{2+} levels, despite minor, possibly undetectable, modifications of the average cytosolic Ca^{2+} concentration.

Keywords: calcium diffusion; mathematical model; microdomains; mitochondria.

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2024Pdm3 March 1 - Abstract 75

Comparison of dysferlin expression in different muscles

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Presentation on site. The author has asked to postpone the submission of the abstract.

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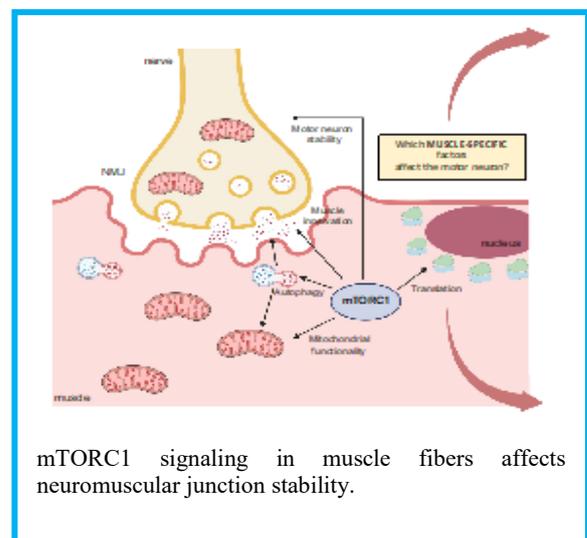
2024Pdm3 March 1 - Abstract 76

The role of Akt-mTORC1 signaling in regulating muscle mass and function

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Loss of skeletal muscle mass and force is of critical importance in numerous pathologies, like age-related sarcopenia or cancer. It has been shown that the Akt-mTORC1 pathway is critical for stimulating adult muscle mass and function. Furthermore, we recently showed that



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mTORC1 signaling during homeostasis in skeletal muscle fibers is also required for maintaining a healthy neuromuscular junction and to maintain muscle functionality. To better understand the underlying signaling changes responsible for this muscle-nerve communication, regulated by mTORC1, we developed new tools to determine changes in the proteome linked to altered mTORC1 signaling. These tools allow us to understand how muscle mTORC1 can affect protein homeostasis and how this is linked to muscle-nerve communication.

Key Words: mTOR, proteome, protein translation, neuromuscular junction, fiber type.

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2024Pdm3 March 1 - Abstract 77

New direction of medical imaging transformation

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This abstract presents an overview of how medical imaging has evolved with the digitalization of healthcare. It highlights the use of DICOM to standardize the storage and sharing of medical images, enabling improved diagnostics and a deeper understanding of physiological conditions. The work focuses on new directions in

medical imaging, specifically in the areas of image segmentation, 3D model rendering, virtual reality, and 3D printing for surgical planning and training. It also mentions the application of virtual histology, medical image features and artificial intelligence to advance clinical assessment and diagnosis. Finally, these advancements in medical image processing technique, highlights the potential impact of these technologies on improving patient care and medical practices.

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2024Pdm3 March 1 - Abstract 78

Redlan: an alternative method for analyzing electromyographic data in orthodontics

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 March 1 - Abstract 79

Dynamic Ecomyography and 3D Muscle Color CT for aging countermeasures: An educational case report

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 March 1 - Abstract 80

Neurophysiology and advanced imaging to investigate muscular morphology and function in adolescent idiopathic scoliosis

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Adolescent idiopathic scoliosis (AIS) is a complex spinal deformity characterized by an abnormal lateral curvature and vertebral rotation of the spine. It primarily affects adolescents during their growth and development. While the structural aspects of AIS have been extensively studied, there is a growing recognition that a comprehensive understanding of this condition should also consider its impact on muscular morphology and function. For this presentation focused on adolescent idiopathic scoliosis and rehabilitation, we conducted a thorough search on PubMed, including trials, reviews, systematic reviews, and meta-analyses published within the last 10 years, with the aim to provide a comprehensive and up-to-date overview of the current state of research regarding muscular morphology and function in AIS. After careful evaluation, we included 127 papers, gathering data on publication year, references to rehabilitation and/or surgery, and various outcome measures. Our findings were visually represented through interconnected pie charts, a bar chart, and a funnel chart, allowing for dynamic visualization. Most of the papers we included in our review focused on surface electromyography (sEMG), while only one delved into evoked potentials. Surprisingly, these electrodiagnostic studies did not explore surgical interventions for scoliosis. Our analysis found no mention of magnetic resonance imaging (MRI) within the sampled articles. Additionally, there was a notable scarcity of electrophysiological assessments for surgical guidance. Our results highlight the need for a more comprehensive evaluation of muscular and sensory pathways, particularly through evoked potentials, which can offer insights into the nervous system's role in the disease's progression and treatment. A multisystem evaluation, particularly when considering muscular function, should become a cornerstone in ensuring effective patient care in the context of AIS.

Key words: neurophysiology; electromyography; scoliosis; rehabilitation.

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Foot drop syndrome: neurophysiological and ultrasound approach in the evaluation of Peroneal nerve (PN) deficit in Rehabilitation.

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The diagnosis of myopathies and neuropathies is of relevant importance in rehabilitation. These pathological entities may present to our attention either in chronic, acute form, or as "Intensive Care Unit acquired weakness" (ICUAW).¹ Peroneal nerve (PN) deficit is commonly found in our clinical practice, it is determined by different etiologies. Thus, since the underlying causes of PN damage are different from each other, a tailored approach to the diagnosis of this condition could allow to prevent it and to set up an effective rehabilitation program. It was also imperative to identify a diagnostic path that could lead to an accurate definition of the patient's prognosis, applying both neurophysiological and ultrasound studies. We carried out a review of the literature to identify the most useful methods, to create a diagnostic pathway that could be easily applicable in any ambulatory care setting. We then identified the following exams: electromyography (EMG), electroneurography (ENG), direct muscle stimulation (DMS) and muscular tissue ultrasound using the modified Heckmatt scale.^{2,3,4} These methods are largely applied in clinical practice as single exams, less frequently in combination. The data collected with each method can be used to obtain various information on the neural conduction, on the neuromuscular junction and the muscular tissue itself. Combining these diagnostic exams, that only require little

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resources and time, could give us enough information,⁴ to ameliorate the allocations of the patient in a rehabilitation setting, creating a tailored program for the patient based on its pathological characteristics.⁵

Key words: myopathies; neuropathies, Rehabilitation, Heckmatt scale; DMS.

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2024Pdm3 March 1 - Abstract 82

Calcium Entry Units (CEUs): dynamic intracellular junctions in skeletal muscle fibers

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Presentation on site. The author has asked to postpone the submission of the abstract.

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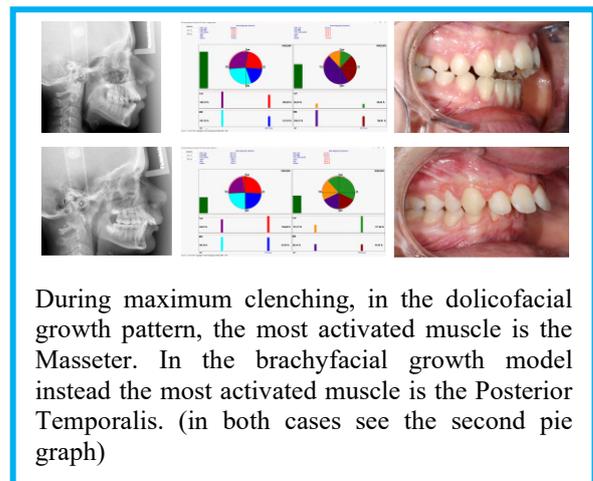
2024Pdm3 March 1 - Abstract 83

Muscle evaluation as an orthodontic prognosis tool

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Orthodontic prognosis deals with defining the facial skeletal growth pattern and the response mode to orthodontic treatment. The skeletal growth model is expressed through a rotation of the upper jaw and mandible which can be clockwise or counterclockwise. The facial pattern connected to the anticlockwise rotation is the brachycephalic one while the clockwise rotation is associated with the dolichocephalic one.¹ Cephalometric morphological analysis on radiography is able to precisely distinguish these two-growth pattern when the facial model diverges significantly from the average. But the sensitivity and specificity of the analysis decreases greatly when the anthropometric measurements are within the range of $\pm 1SD$, especially when the patient is pre-adolescent. Electromyographic analysis can help in



the differential diagnosis between these two growth modalities by postulating a different way of using the mandibular elevator muscles by these two different facial morphologies. This diversity is detectable and quantifiable through a simultaneous recording of the muscular activity of the Masseters (MM R&L), of the activity of the anterior part of the Temporalis (TA R&L) and of the activity of the posterior part of the Temporalis (TP R&L) expressed in the maximal voluntary clench (MVC). The value of the differential activation index ATT between masseters and temporalis is measured separately for the two pairs TA/MM and TP/MM.^{2,3} The positive or negative value and the absolute value of both activation indices allows us to functionally differentiate the two skeletal growth patterns. The electromyographic analysis and the cephalometric

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morphological analysis are usually congruent and allow us to accurately predict the evolution of growth even when the case in question has cephalometric values close to the average. This observation is congruent with the functional matrix hypothesis according to which there would be a different form-function relationship in the two patterns of facial growth.⁴

Key words: surface electromyography; facial growth; form and function relationship; orthodontic treatment; prognosis in orthodontic treatment.

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2024Pdm3 March 1 - Abstract 84

TMD: Clinical Implications for the Orthodontist

Giacomo Begnoni

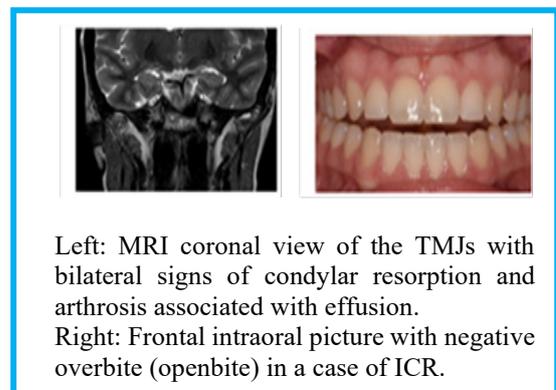
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Temporomandibular disorders (TMD) encompass a group of musculoskeletal and neuromuscular conditions that involve the temporomandibular joint, the masticatory muscles and the associated tissues with a reported prevalence of up to 45% for muscle pain, 41% for disc derangement disorders, and up to 30% for joint pain disorders. Historically, patients with TMDs are often referred to the attention of orthodontic specialists as the symptoms are often misdiagnosed and attention is often diverted to morphologic aspects secondary to the

management of the patient's reported complaints. The orthodontist is thus faced with cases where the clinical management can be complex from an orthodontic point of view, and unsatisfactory in terms of symptoms resolution, with a consequent inevitable frustration for both the patient and the caregiver. Identifying patients with TMD is therefore crucial in planning (or not) an orthodontic treatment. Aetiology, diagnostic criteria and treatment modalities are reported through the presentation of clinical cases of patients with TMD referred to the department of Orthodontics at the University Hospital of Leuven (Belgium).

Key words: temporomandibular disorders; orthodontics; muscle pain; dental occlusion.



Left: MRI coronal view of the TMJs with bilateral signs of condylar resorption and arthrosis associated with effusion.
Right: Frontal intraoral picture with negative overbite (openbite) in a case of ICR.

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History and perspectives of translational myology

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Once upon a time Giovanni Vincenzo Borelli that was a man of science (also catholic bishop)¹ wrote a superb book: "De motu animalium" a splendid text for his modernity. In the «De motu animalium» (1680), you can find the exact decryption of what happens to induce and develop muscle contraction.

In the book it is possible to read:

1. To produce muscle contraction, there are two causes of which one exists in the muscles (contractile proteins) and the other comes from outside (nerve impulse).
2. the impulse to movements can not be transmitted from the brain by other means than by the nerves; and the experiences are moreover evident in this;
3. therefore it is necessary to admit that some bodily substance, a "pungitiva acredine" (the neurotransmitter Ach) spreads to the end of the nerve to irritate the muscle;
4. and that a "commotion" (action potential) is created which can in a blink of an eye (E-C coupling) produce the swelling of the muscle (contraction)".

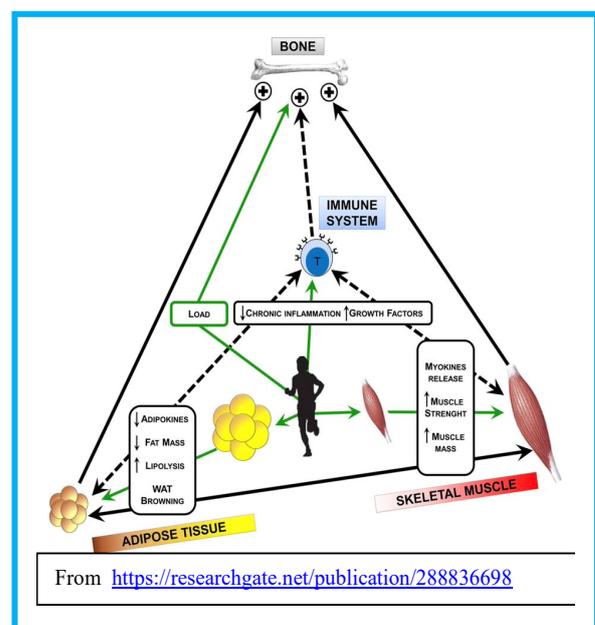
More than 200 years later, a laboratory mistake marked the beginning of the Ca²⁺ era in muscle contraction. Sidney Ringer in the 1883 (*J. Physiol.*4, 29-43, 1883) had suspended frog hearts in a saline solution for which he admitted that he had used, by ERROR, the tap water in London that was rich in calcium in place of distilled water.

Under these conditions the heart had continued to beat for many hours while this did not occur if distilled water or other calcium-ion-free solutions were used.

At the beginning of the 20th century, Emilio Veratti published the description of an elaborate form of reticulum (SR) in skeletal muscle fiber but the results of his paper did not have an adequate diffusion. Veratti's work was rediscovered by Stanley H. Bennett and Keith

R. Porter, who took care of the republication in English in 1961. Today, we know precisely which reticular structures are capable of coupling the excitation of the muscle membrane with the fibre contraction (Protasi and Franzini-Armstrong 1998). Another fundamental passage occurs in the mid 50s of the last century. In fact, 1954 was a memorable year for myology because it was proposed by A.F. Huxley and Niedergerke as well as H.E. Huxley and Hanson, at the same time and on the same issue of Nature,² the theory of sliding filaments to explain muscle contraction. A few years later, Annemarie Weber showed that very low concentrations of Ca²⁺ (µM) are necessary to induce ATP hydrolysis in actomyosin substrates and Ebashi and Kodama identified the target for the calcium ion on the thin filaments the calcium binding protein, troponin C. Thus, the main structures and muscle contraction protagonists were known. In the early 1970s, the systematic study of the specificity of the proteins that make up the fast fibres began. Mammalian skeletal muscle comprises different fiber types, whose identity is first established during embryonic development by intrinsic myogenic control mechanisms, and is later modulated by neural and hormonal factors.

A complete analysis of this scenario was described in great detail by Schiaffino et al (*FEBS J.* 2013) a few years ago. But myogenesis is not only an embryonic phenomenon because it also occurs during adult life thanks to the presence of stem cells that were first identified by Alexander Mauro in a memorable paper of only three pages and without co-authors describes for the first time the presence of satellite cells which are located between the basal lamina and sarcolemma of individual myofibers (*J Biophys Biochem Cytol.* 1961). The myogenic capacity is so strong that even muscles reduced to less than 10% of their initial volume by prolonged



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denervation can regain mass through continuous stimulation.³ The muscle, if it has no load and / or innervation, undergoes processes of atrophy (autophagy) that directly involve the lysosome by the transcription network of the FoxO factor as showed also by Sartori and Sandri (Nat Commun. 2021) in these last years.

The fundamental importance of physical exercise in slowing down muscle decay or facilitating recovery after debilitating diseases is now well established in the management of both sarcopenia related to oxidative stress (Fanò-Illic G, Fulle S. Antioxidant 2022) and post-infectious phases such as ME/CFS or Long Covid (Coscia et al EJTM 2023). In the new millennium, skeletal muscle is also considered an endocrine tissue. Clear evidence has emerged that the cellular components of skeletal muscle are important sites for the release of proteins and peptides called "myokines", suggesting that skeletal muscle plays the role of a secretory organ able to act with effects autocrine, paracrine, endocrine.⁴

In particular, several skeletal-muscle secreted myokines, facilitates muscle-bone crosstalk and skeletal remodeling in part by its action on osteoblasts and osteocytes. This concept of muscle-bone crosstalk at a molecular level is particularly interesting in the mandible, due to its tight anatomical relationship with one of the biggest and strongest masticatory muscles, the masseter. On other hand, one must take into account that the masticatory system is a complex and highly organized group of structures, including craniofacial bones (maxillae and mandible), muscles, teeth, joints, and neurovascular elements (Koolstra, Crit Rev Oral Biol Med. 2002).

By analysing the pathophysiological implications of myokine induced muscle-bone crosstalk in the masticatory system, it is conceivable that defining the mechanisms of muscle-bone interchange in the masticatory system will open up a new scenario for understanding and treating temporomandibular disorders, which severely impair the patient's quality of life, with high costs for diagnosis and management.⁵

Key words: muscle history; myogenesis; myokines; muscle-bone cross-talk; masticatory muscles.

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Oral care for the patients with xerostomia and hyposalivation in systemic diseases

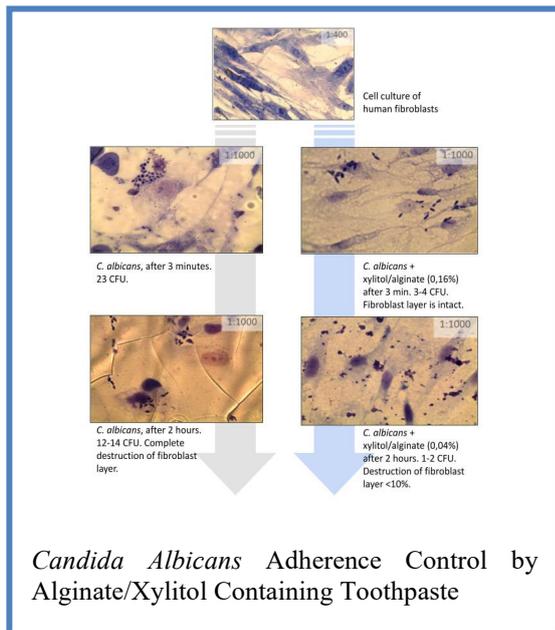
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Diabetes mellitus (DM) is an endocrine disease in which insulin production is reduced or absent or the sensitivity of cells to Insulin is impaired (insulin resistance), which leads to inappropriately high levels of glucose in the blood - hyperglycemia. DM aggravates the dental status of patients. One of the first complaints is a subjective feeling of dryness in the mouth - xerostomia. It may be associated with thirst (due to dehydration caused by polyuria), sensory dysfunction (as a result of peripheral neuropathy), changes in the qualitative composition of saliva, or dysfunction of the salivary glands leading to an objective decrease in salivary secretion (hyposalivation). Xerostomia can also be a side effect of medications used to treat diabetes. Not all patients who complain of dry mouth have hyposalivation. The degree of hyposalivation is reported to correlate with the level of glycosylated hemoglobin (HbA1C) in the blood.¹ Reduced saliva secretion leads to disturbances in speech, chewing and taste perception. Moreover, the protective function of the

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oral fluid in conditions of hyposalivation is compromised. Other oral conditions associated with diabetes mellitus include poor hygiene indices, a higher risk of caries and periodontal diseases, etc.² To alleviate xerostomia and protect the oral mucosa in patients with diabetes mellitus, it is advisable to use specialized oral hygiene products that have a moisturizing effect. Promising results have been shown in clinical studies of toothpaste containing potassium alginate and xylitol. When using the specified combination of components, an improvement in hygiene indices and a stimulating effect on salivation in patients with xerostomia and hyposalivation associated with type II diabetes mellitus have been shown.³ Moreover, the use of toothpaste with xylitol and alginate can alleviate the severity of mucositis in children receiving combination chemotherapy for cancer.⁴ Regarding control of microbial adhesion, the ability of xylitol/alginate containing toothpaste to prevent the adhesion of *Candida albicans* fungi to cultures of human myofibroblasts is of great importance.⁵ The report will present clinical cases of the use of toothpaste containing xylitol and alginate in patients with diabetes mellitus and comorbid pathologies.

Key words: diabetes mellitus; xerostomia; hyposalivation; candida albicans; xylitol alginate toothpaste.

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Orthopedic-orthodontic therapy of transverse expansion of the palate: is the adaptation of the masticatory muscles possible and in how long time?

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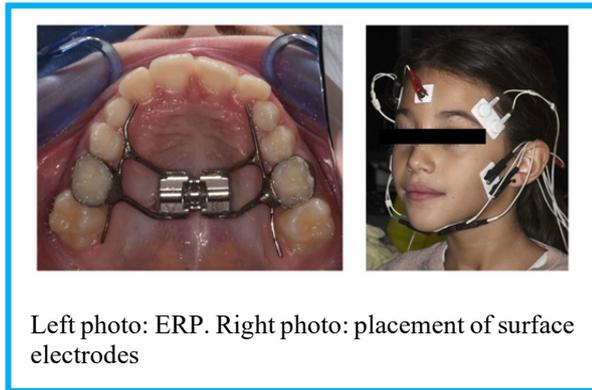
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Rapid palatal expansion is a widely accepted procedure and is recommended to correct maxillary constriction, in particular related to posterior crossbite. Opening of the median palatine suture promotes the increase of maxillary width and dental arch perimeter, but its effects on the neuromuscular system are not clear yet. Electromyography (EMG) is a noninvasive exam which evaluates the masticatory muscle activity by facial application of electrodes on masseter (MM) and anterior temporalis (TA) muscles. The aim of this prospective clinical study is to analyze electromyographic activity of MM and TA in maximum voluntary clenching (MVC) in patients undergoing maxillary expansion with rapid palatal expander (RPE). Standardized surface electromyography was used to evaluate the activity of the masticatory muscles (MM and TA) before the beginning of the orthodontic treatment with RPE (t0), at the end of expansion (t1), and 6 months (t2) after the end of the

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Left photo: ERP. Right photo: placement of surface electrodes

activation of the RPE. 22 healthy patients were recruited (9 boys and 13 girls) aged 6 to 17 years with maxillary contraction. 20 completed the protocol while 2 performed only the first 2 measurements. The data gathered were evaluated with repeated measurements analysis of variance (ANOVA test). Results did not show statistically significant differences of the analyzed electromyographic indices, before and after RPE. Although there was no statistical significance, the main indices showed a reduction at t1, compared to t0, but at t2 EMG activities increased again. These preliminary results show that RPE appears neutral on the neuromuscular system, although further studies are needed to either confirm or deny this hypothesis.

Key words: surface electromyography; masticatory muscles; rapid palatal expansion.

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An interdisciplinary approach in clinical-instrumental evaluation of motor skills in athletes with disabilities

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It is estimated that only 4-6% of people with disabilities participate in regular physical activity on the national territory. There are still too many young people who experience their disability mainly in the family context and contacts in society are often represented by medical visits, school attendance and IT channels; Reassuring environments for parents, but which risk increasing or reinforcing the concepts of disability, dependence and diversity in them. Addressing the world of Disability in Sport, where physical, mental and neurosensory problems often coexist, requires an interdisciplinary approach for a better clinical-diagnostic and therapeutic framework of athletes. The various disabilities require an adequate refinement of our knowledge so that it is useful for improving the residual abilities of these athletes. The occlusal component can be caused or adaptations in the complex system of postural control and clinical evaluations involve an in-depth and multidisciplinary knowledge of the systems that govern it, in order to implement the most appropriate therapeutic strategies to improve the athletic gesture. The exteroceptive component of the eye is integrated into a complex postural tonic system, which includes the vestibular, gnathological and proprioceptive breach systems, allowing constant adaptation in both static and dynamic conditions. Athletes, both able-bodied and Paralympic, are usually subject to logistical movements, have lower sporting performance related to poor sleep quality and eating disorders. The SIOS (Italian Society of Sports Odontostomatology) follows athletes with disabilities with particular attention, proposing a clinical-instrumental approach dedicated to the study of the main postural receptors and problems relating to the

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prevention of oral health, dental-facial trauma, correct nutrition and sleep disorders.

Key words: oral health; salivary factors; disability; osas.

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Speech therapy in dental treatment plan

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One system (stomatognathic system), two specialties (dentistry and speech therapy) and a common objective: seeking balance in the relationship between dentofacial morphology and orofacial functions. From this perspective, interdisciplinary work has become increasingly relevant in clinical practice. In the literature it is possible to find several studies considering the interdisciplinarity between dentistry and speech therapy. Some of them highlighted interdisciplinary work between Speech Therapy and areas of Dentistry.¹⁻³ The interaction of speech therapy treatments with dental patients usually goes beyond inappropriate tongue behavior or “atypical” swallowing. There are several functional difficulties that occur, unbalancing the morphology and the function in the stomatognathic system. They can present themselves as a cause or a consequence of changes in dentofacial morphology and even as a consequence of the dental intervention. Among them, we can mention: presence of oral habits, altered swallowing, altered tongue positioning, difficulties with chewing, changes in breathing, difficulties with speech articulation after the installation of the device, functional re-education after prosthetic rehabilitation, functional balance for treat orofacial pain, etc. In an ideal world, speech therapy and dentistry, joining forces, seek early diagnosis and therapeutic planning with greater benefits for patients. In the real world, knowledge and points of convergence between these two areas are not always well defined. There are some issues that are not completely clear to both professionals. This makes interdisciplinarity hard, in the daily activities of each of them. It is still common for many professionals to question when and how to refer a patient; what the speech therapist can do in different cases; what is the hierarchy of treatments; how to articulate the knowledge and practices of each of these two specialties to offer a better structured and effective treatment. In this sense, it is necessary that each of the professionals (dentist and speech therapist) knows the objectives and benefits of the treatment proposed by each team member. That is, the view of the case should not be purely speech-language pathology or purely dentistry, but interdisciplinary. Nor should this interdisciplinarity be casual or for convenience, but the most interesting thing is that it be fluid and everyday. Only with the necessary knowledge

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and constant interdisciplinary interactions can we create more well-established and effective prevention and (re)habilitation behaviors. In some countries, the Speech Therapist specialty is the professional responsible for treating patients with orofacial myofunctional disorders, through orofacial myofunctional therapy. This is a treatment based on exercises, which aims to promote proprioception, tonicity, and mobility, working with the facial and cervical muscles and also with stomatognathic functions – breathing, chewing, swallowing and speech, although, this application has been suggested and applied in different cases, with results demonstrating a reduction in the symptoms of temporomandibular disorders,⁴ snoring and obstructive sleep apnea,⁵ in orthodontic cases,³ among others. In these cases, there seems to be a consensus that the essential role of the speech therapist is to promote the stability of the treatment carried out by orthodontists, functional jaw orthopedists and/or pediatric dentists, especially preventing recurrences. This lecture aims to present situations which clinical monitoring by professionals in both speech therapy and dentistry is recommended. Finally, make both professionals aware that orofacial myofunctional treatment should be part of a daily collaboration plan in the search for balance in the stomatognathic system.

Keewords: interprofessional relations; dentistry; speech therapy; myofunctional therapy.

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Malocclusion and Scoliosis: is there a correlation?

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Scoliosis is a complex three-dimensional deformity of the spine. Studies of scoliosis show evidence of the existence of three components: frontal, sagittal, and axial. Its etiology is still under analysis, but it is evident that there are various causes that can determine this condition. From an etiopathogenetic point-of-view, the spinal deformity caused by idiopathic scoliosis may be defined as a sign of a complex syndrome with a multifactorial etiology. Its connection with malocclusion is confirmed by several studies, but until now it has not been well understood how these aspects influence each other. Malocclusion is an alteration of the physiological relationship between the upper and the lower teeth that can be classified as either dental or skeletal. The aim of this study is to evaluate the correlation between scoliosis and malocclusion. We enrolled 646 patients (554 females and 67 males), 447 with scoliosis and 177 without, from private dental and orthopedic practices, where they all had a dental examination and an orthopedic analysis, and who answered to an anonymous questionnaire. The study adds further confirmation that there might be an important connection between malocclusion and scoliosis. It suggests that dentists and orthopedists be advised to check, as early as possible, for the probable presence of both pathologies to avoid a severe progression which, in most cases, may require significant therapy and even surgery. We will highlight the important presence of temporomandibular/orofacial pain disorders in patients affected by scoliosis, with a higher frequency than in the ones who are without this spinal deformity.

Keywords : scoliosis; malocclusion; TMJ; orofacial pain; tongue posture.

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2024Pdm3 March 2 – Abstract 91

Mimicking short-term immobility and early rehabilitation in an animal model

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 March 2 - Abstract 92

Insights into muscle atrophy and sarcopenia: mechanisms and countermeasures

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 March 2 - Abstract 93

Determinants and predictors of muscle mass, function and mobility: cross sectional study in young and old muscle

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In the last decades, the extended human longevity resulted in increasing numbers of senior individuals in the general population, and interventions focused to the maintenance of muscle mass and strength are important for an active ageing linked to a healthy ageing. Aging is a multifactorial process that is influenced by immunological, hormonal, and nutritional factors. With age, the reduction of muscle mass, strength and resistance are typically observed.¹ Muscle disuse due to sedentary lifestyle of elderly accounts for frailty and fragility and it is clearly associated with an impaired structure and function of the musculoskeletal system. Several studies revealed that in the older people the muscle weakness of the lower extremities or the reduction in balance and mobility capabilities, are major factors contributing to falls in these people. Falls can lead to bone fractures, that are associated with physical disabilities, reduced quality of life, increased mortality, and rise in health care costs. Physical exercise represents a good option invoking a mixture of metabolic, hormonal, neural and mechanical stimuli that can altogether contribute to the improvement of skeletal muscle morphology and performance, also enhancing the quality of life of trained elderly subjects.² The 2020 WHO guidelines for physical activity in young adults and old populations is to perform 150-300 minutes of multimodal program of moderate and/or 75-150 minutes of vigorous-intensity physical activity per week.³ In the present study, we examined the effects of physical activity in young adult and in ageing with respect to muscle morphology, ultrastructure, and gene expression, strength and mobility parameters, cardiorespiratory fitness, and circulating biomarkers of inflammation and neuromuscular junction stability. Four groups of young adult and seniors stratified by age and their level of physical activity above and below the WHO recommended range participated to the study.⁴⁻⁶ Descriptive statistics, correlation and linear regression analyses of all collected data were performed in order to identify determinants and potential predictors of muscle mass, strength, and mobility.

Key words: ageing; muscle loss; physical exercise; strength; mobility.

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2024Pdm3 March 2 - Abstract 94

Water therapy: its place in rehabilitation and opportunities for optimisation

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 March 2 - Abstract 95

Results of a new model of rehabilitative transitional care for geriatric patients

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 March 2 - Abstract 96

Improved mentalizing is a protective factor against depressive symptoms and pain severity in patients with chronic rheumatic pain

David Riedl,

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 March 2 - Abstract 97

Is Isokinetic Dynamometry a useful assessment for physical function post- knee and hip arthroplasty?

Ferdinand Prüf

LBI Rehabilitation Research, Vienna, Austria

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2024Pdm3 March 2 - Abstract 98

Comparing rehabilitation programs using different types of outcome measures

Špela Matko

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Critical success factors in orthopedic rehabilitation - from the perspective of patients and doctors

Chiara Vetrano

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Presentation on site. The author has asked to postpone the submission of the abstract.

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2024Pdm3 March 2 - Abstract 100

Balance control recovery by healing or by compensation in sensory and osteoarticular pathologies after hydrotherapy

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Within the framework of studies set up in Nancy, France - twinned with Padua, Italy -, Nancy once again becoming a Thermal Spa, are presented the part of these studies, linked to the evaluation of postural control, that has been done, is being done and is planned.

Postural control, which is an integral part of many ordinary activities, is a complex sensorimotor function that requires central integration of visual, vestibular, and proprioceptive/somatosensory systems. Integration of these inputs generates a context-specific motor response, which leads to stabilization of gaze and antigravity posture. The weight and hierarchy of these sensory inputs, and therefore balance strategies, vary according to subject, age, learning and experience (sports), particular situations [environment, vigilance (i.e. sharing of attentional resources in multiple tasks)], pathologies and their treatment modalities. Following the onset of a sensory or osteoarticular pathology, balance control may be regained through healing or compensation. Treatment with hydrotherapy can help to facilitate the mechanisms of recovery through healing. Hydrokinesitherapy uses the physical and chemical properties of water to help heal patients suffering from certain osteoarticular and neurological diseases. In the aquatic environment, Archimedes' principle (describing the upward buoyant force that is exerted on a body immersed in a fluid) enables a patient to be supported more easily. Hydrostatic pressure also helps to counter oedema. Warm thermal water has an analgesic effect. Mobilisation is facilitated, muscles strengthening is secured and somesthetic work is intensified by the aquatic environment. For the above reasons, physical properties of water in balneotherapy have also been shown to improve postural control by reinforcing proprioceptive input and increasing muscle

Hydrokinesitherapy – Nancy Thermal

- Archimedes' principle: reduced gravity
=> Earlier support
- Hydrostatic pressure
=> Effective action against oedema
- Warm thermal water
=> Analgesic effect
- Easier mobilisation
- Secure muscle strengthening
- Somesthetic work intensified by the aquatic environment.



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strength. Hydrostatic pressure associated with viscosity increases exteroceptive sensory input, allowing for better limb perception. After cruciate ligament rupture of the knee, the benefits of rehabilitation in a thermal environment after ligamentoplasty have been shown, with recovery by healing in a thermal environment compared with compensation using the contralateral knee in dry rehabilitation. Overuse of the contralateral knee can lead it to a risk of cruciate ligament rupture in the medium term, and knee osteoarthritis in the long term.¹ Land-based exercise and balneotherapy are currently used to decrease some symptoms related to knee osteoarthritis in a non-pharmacologic approach. High-frequency intensive balneotherapy (three weeks standardized continuous balneotherapy) improved posture control at three weeks, while low-frequency balneotherapy (discontinuous frequency, three days a week) did not. This improvement persisted over a 12-week assessment period at the same level. Land-based exercise generated an improvement that did not persist over time. Sustained improvement of postural control requires high-frequency repetition of consecutive balneotherapy sessions.²⁻⁴ Postural instability and loss of vestibular and somatosensory acuity are among the signs seen in Parkinson's disease. Visual dependency and decrease in performance on tasks that need multisensory integration are also described. Our study had suggested that Parkinson's disease patients do not have increased real induced motion sickness susceptibility, but are susceptible to some visual-induced motion sickness in provocative situations (moveable posturography platform with virtual reality environment). This difference can be explained by a high reliance on visual input and a low performance of vestibular and somatosensory inputs. If stimulation aimed at habituating to a specific disturbing situation can help to desensitize a patient to visual-induced motion sickness, strategies such as practicing physical activities that modify the sensory input hierarchy, increasing somatosensory weighting, could be effective at decreasing visual overreliance and reduce the risk of falling that can be the result of such a visual reliance.⁵ After arthroscopic repair of the shoulder rotator cuff, it would seem appropriate to consider post-operative rehabilitation in a hydrotherapy environment. In the case of the compensatory mechanism put in place in the rotator cuff, this is a model where this mechanism can involve recourse to the same region (i.e. the shoulder), but using the joints in a different order to orchestrate these movements. This mechanism is therefore different from the compensation mechanisms put in place when other neurosensory or osteoarticular structures are affected: compensation for vestibular damage by the contralateral vestibule, by vision and/or proprioception, compensation for knee damage by the contralateral knee, etc. Biomechanically, physiological abduction of the shoulder is achieved by the action of the

five joints of the shoulder joint complex in harmony. In the event of a deficit in one of these joints, a compensation mechanism will take its place in performing this movement. In the case of a cuff tear, in particular, the movement of the glenohumeral joint will be replaced by that of the scapulothoracic joint. In addition, from a postural point of view, in a recovery by compensation compared to a recovery by healing, a postero-lateral shift (contralateral to the lesion) of the centre of foot pressure can be observed when the upper limb is raised anteriorly above the level of the head.

Balance control presents varying difficulties depending on the activity and will be much difficult to ensure during movement as it will tend to shift the centre of gravity further in particular situations encountered in certain professional or sporting activities. In an aquatic environment, compared to conventional dry care, recovery can be achieved more frequently by healing, rather than compensation, which is more appropriate to life situations, and accordingly to a patient's well-being. Key words: sensory and osteoarticular pathologies; recovery by healing; recovery by compensation; hydrotherapy.

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Can optimized human home-based Full Body In-Bed Gym induce functional and structural improvements in octuagenarian muscles? Functional and structural evidence.

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Except for world record holders on record day, all other people never express the full value of their potential performance due to the obvious detraining condition secondary to a sedentary lifestyle. Therefore, initiating training programs, particularly in elderly stage is very likely to provide small or large improvements. One of us began a more active lifestyle at age of 70 years, after retiring from a sedentary lifestyle as teacher at the University of Padova, Italy. He is still improving after 10 years of performing a short bodyweight program immediately after waking up, specifically performing this program lying down, sitting up and out of bed for no more than 20 minutes, but almost every day. He continues to gauge the strength of his arm muscles by counting the number of push-ups he can do while lying in the floor. During last summer, autumn and winter he continued to improve his record from 20 to 30 push-ups. Clinical imaging will show that structurally the muscles of the body are almost the same as they were ten years before. This is combined with psychological benefits. Therefore, starting from a detraining condition it seems to be possible to stop the physiological decay linked to aging, if not to rejuvenate. In conclusion, the home-based, every-day, Full-Body in-Bed Gymnastic is an easy-to-learn-and-memorize, economical and not time-consuming way to maintain a better quality of life.

Key words: Full-Body in-Bed Gymnastic; function and structure of muscles; quality of life.

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Effect of intensive rehabilitation program in thermal water on a group of people with Parkinson's Disease: a retrospective longitudinal study

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Physical therapy hampers the impact of motor symptoms in daily life activities (ADL) of people with Parkinson's disease (PD, PwP), but effectiveness on non-motor symptoms is still debated.¹ Aquatic exercise reduces the risk of harm during therapies and water viscosity represents a cue for PwP.^{2,3} Moreover, thermal environment promotes muscle relaxation and endorphins production.⁴ This research aims at investigating the effect of thermal aquatic exercise on motor and non motor symptoms in PwP. 18 participants with idiopathic PD met the inclusion criteria (Hoehn & Yahr in OFF-state: 2-3; Mini Mental State Examination > 24; stable pharmacological treatment). Cognitive and motor status, functional abilities and quality of life were assessed at baseline and after an intensive rehabilitation program in thermal water (12 sessions of 45 min in a 1.4 m depth pool at 32-36°C). The Mini Balance Evaluation System Test (Mini-BESTest) and the PD Quality of Life Questionnaire (PDQ-39) were considered as main outcomes. Secondary assessment measures evaluated motor and non-motor symptoms. Participants kept good cognitive and functional status after treatment. Motor status of all the participants significantly improved (Mini-BESTest: $p < 0.01$). The PDQ-39 significantly improved after rehabilitation ($p = 0.038$), with significance being driven by dimensions strongly related to motor status. In conclusion, thermal aquatic exercise prevents the impact of motor symptoms on ADL of PwP. Moreover, PDQ 39 improvement foreshows good effects of the intervention on non-motor symptoms.

Key words: Parkinson's disease; physical therapy; aquatic therapy; motion analysis.

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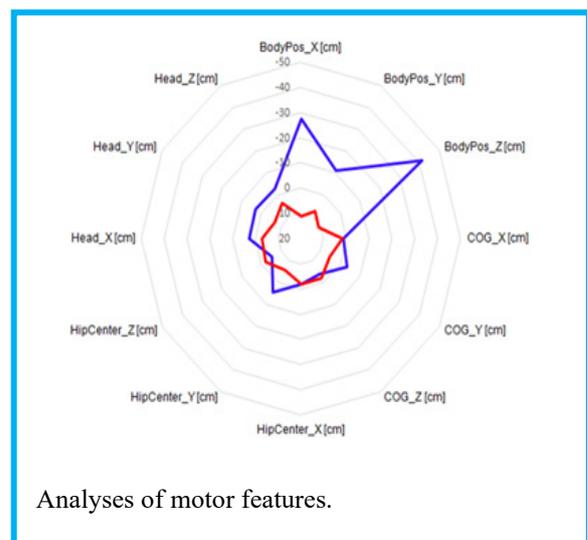
Dynamic control of motor disorders in the early stages of Parkinson's disease

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Diagnosis and treatment of Parkinson's disease (PD) remains one of the most significant problems of neurology today. Parkinson's disease prevalence is increasing with age and PD affects more than 1% of the population above 60 years. Parkinson's disease is characterised by a large number of motor and non-motor features. Motor deficits generally appear when 50-60% of dopaminergic neurons in the substantia nigra are already lost, limiting the effectiveness of potential neuroprotective therapies. Taking into account the substitutive symptomatic therapy of this pathology, it is very important to have the monitor the adequacy and effectiveness of the treatment. In our study a non-contact system of objective assessment of movements is used for estimation of the motor symptoms. An objective analysis



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of the structure of motor and non-motor symptoms will allow for a more reliable diagnosis at an early stage of Parkinson's disease. Comprehensive monitoring of the effectiveness of treatment of motor and non-motor disorders in the early stages of Parkinson's disease will improve the quality of life of patients, expand the possibilities of social adaptation.

Key words: Parkinson's disease; early diagnosis; non-motor symptoms postural control.

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Functional asymmetry of the brain: an innovative test for left-handedness and leftness in neurorehabilitation,

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Fast and high-quality detection of leftyness can be very informative in pedagogy, professional selection, medicine. To do this, it is necessary to develop a test that should be informative, simple, concise, quick to conduct and calculate, not requiring special equipment, combining questions and tasks, revealing mainly persistent and unambiguous manifestations of leftyness in various aspects such as biographical, motor, sensory,

mental ones (1,2,3). Goal: to develop a universal test that provides reliable and rapid detection of signs of leftyness in healthy and sick subjects. Materials and methods: according to the developed protocol for leftyness detecting, consisting of 13 questions and samples, 210 people were studied, including 100 healthy persons and 110 patients randomly selected during neuropsychiatric or neuropsychological examination. Results: test providing and protocol completion were fast, easily accessible both in the study of health and patients. When testing the primary protocol, it was found that: a) patients older than 30 years were less likely to report the presence of signs of leftyness, most of them preferred the right hand; b) women, compared with men, were more likely to report the presence of prophetic dreams and other variants of foresight; c) familial leftyness was more often found in patients compared with healthy persons d) according to most of the studied signes (7 out of 13), the largest proportion of patients with leftyness was found in patients with functional mental illnesses; e) significant correlations were found between biographical leftyness and left-handedness, as well as between left-handedness and ear leftyness. Based on the conducted research, a new improved protocol of test for the express detection of signs of leftyness (TEDSL) was created. The modified TEDSL protocol developed as a result of this work is ready for use in further studies of various contingents of healthy and patients with various psychopathological symptoms.

Key words: functional asymmetry; leftyness; left-handedness; testing.

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2024Pdm3 March 2 - Abstract 105

Mitochondrial dysfunction, stress, innate immune activation and Inflammation: «Black Square» in the pathogenesis of neurodegenerative diseases

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Neurodegenerative diseases include a fairly extensive group of diseases characterized by progressive death of nerve cells, which leads to deep violations of cognitive and motor functions. Among these diseases, Alzheimer's (AD) and Parkinson's (PD) diseases associated with old age occupy a special place in terms of social significance, due to the high prevalence and level of disability. The development of these pathologies is based on a violation of the metabolism of individual neuropeptides: the accumulation of pathological tau protein molecules with the formation of neurofibrillary glomeruli and amyloid plaques in AD and the intraneuronal expansion of pathological phospho- α -synuclein in AD (1). Thus, under chronic stress, a certain inflammatory background is formed, complementing (enhancing) the "pro-inflammatory status" that develops as a result of age-related changes in the immune system and disruption of mitophagy mechanisms. According to some authors, the development of proinflammatory status is the result of prolonged (chronic) influence of stress factors, which leads to a violation of the homeostatic connection between the neuroendocrine and immune systems (2,3,4). Thus, the development of age-related neurodegenerative diseases is based on neuroinflammation, in the formation of which three closely related groups of factors contribute: mitochondrial dysfunction, primarily associated with impaired mitophagy processes, chronic emotional stress, and age-related inflammatory imbalance of the immune system.

Key words: biopsychosocial approach; stress; neurodegenerative diseases; aging.

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Methodology for predicting the therapeutic effect of an area

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The aging population of developed countries, increasing life expectancy, high motivation to maintain active working life, leads to an increase in the share of sanatorium-resort treatment in the market of health services. The development of the methodology will make it possible to select the optimal location and season depending on the combination of local conditions and microclimate and predict a reduction in the risk of complications. The inclusion of the NDVI parameter as an indicator of greening was necessary, since green spaces provide a flow of negatively charged particles, phytoaromatic substances and phytoncides. A pilot study was conducted, which included 40 conditionally healthy volunteers (19 men and 21 women, their median age was 60.0 years, age range was 53.0; 64.0 (LQ, UQ)). The study was conducted over 10 days of June 2021 in Moscow (55°66'21" north latitude 37°67'06" east longitude). The impact consisted of conducting a health path course (10

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procedures) for 30 - 40 minutes, 6 days a week, during the day at 12 o'clock, along a constructed route of 1000 meters. The training was carried out with a load and a pace of medium intensity. The training was carried out no earlier than 2 hours after eating, the volunteers had to adhere to the drinking regime. The route of the path was laid through open areas, in close proximity to a mixed forest (50 meters) and green spaces (willow, rowan, juniper). On this route, studies of local air temperature, relative air humidity, and atmospheric pressure were carried out using the Gismeteo.ru website and a portable weather station (Meteoscope-M, Russia). The measurements were carried out at a distance from the surface of the earth - 1 meter in the summer of 2021, from 10 am to 1 pm in the route area. Data on the NDVI vegetation index were taken from the Earth Explorer website [Earth Explorer [Electronic resource] // URL: <https://earthexplorer.usgs.gov.html>]. The slope angle of the health path route was measured using a leveling device.

Before and after the health path course, a study of the microcirculatory bed was carried out using LAZMA-PM (LLC NPP LAZMA, Russia). Nonlinear logit regression was used to estimate the model using the maximum likelihood method. The dichotomous function of this logistic model was normal or altered oxidative metabolism (POM). The qualitative assessment of the model was calculated as the odds ratio (1).

The probability was calculated using the formula (2):

$$p = 1/1+e^{-z}, \quad z = b_1*x_1+b_2*x_2+\dots+b_n*x_n+a$$
 (2)

where x_1 – values of independent variables; e – mathematical constant equal to 2.71828; b_1 – regression coefficients of logistic regression, calculated when constructing the model; a – constant.³

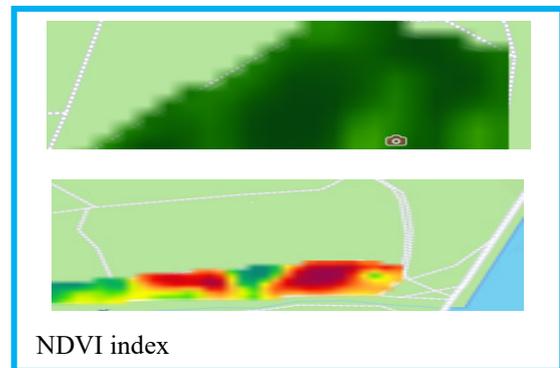
An increase in P (probability) of more than 50.0% indicates a decrease in the likelihood of the onset of metabolic pathology (spasmodic or stagnant), since the sample contains more patients with a normal vascular response to the health path.

Statistical analysis of the data was carried out using the Statistica v program. 8.0 (StatSoft Inc., USA) and Microsoft Excel (Microsoft, USA). The significance of the differences was considered established at $p < 0.05$. Based on the data obtained, using logistic regression, we built a model. Model (3):

$$p = 1/1+e^{-z}, \quad \text{where } z = 3,733NDVi * x_1 + 1,738t * x_2 + -0,082Patm * x_3 + 0,394humidity \text{ rel} * x_4 + -0,122relief \text{ slope} * x_5 + -0,013age * x_6 + 0,5sex * x_7 + 2,588 \text{ (a constant)}$$

Let us indicate the symbol of the factors included in the calculation: (1) NDVi index (NDVi); (2) daytime air temperature (t); (3) atmospheric pressure (Patm); (4) relative air humidity (humidity rel.); (5) terrain slope (relief slope); (6) age; (7) sex.

Model parameters: maximum likelihood index of the model is 26.5; intercept was 55.64; $\chi^2=29.14$; $p=0.0001$; OR=35.75; 95% CI – 5.73–223.01. Sensitivity was 76.5% and specificity was 91.7%. The overall accuracy of the predictive model is 85.4%.



It was revealed that the greatest contribution to the risk of developing microcirculatory disorders is made by a low NDVI index, an increase in air temperature and atmospheric pressure. Online monitoring using wearable devices will allow you to individualize the dosage of physical activity and move to an “electronic climatotherapy prescription”, increasing the safety, efficiency and personalization of spa treatment. The inclusion of climatotherapy in the sanatorium-resort phase in areas with diverse landscapes can have a positive effect only if it is used in target groups and prevents the occurrence of meteoropathic reactions.

Key words: climatotherapy; online monitoring; NDVI index; microcirculation; sanatorium-resort.

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Additional pharmacological therapy for epilepsy with drugs unrelated to anticonvulsants

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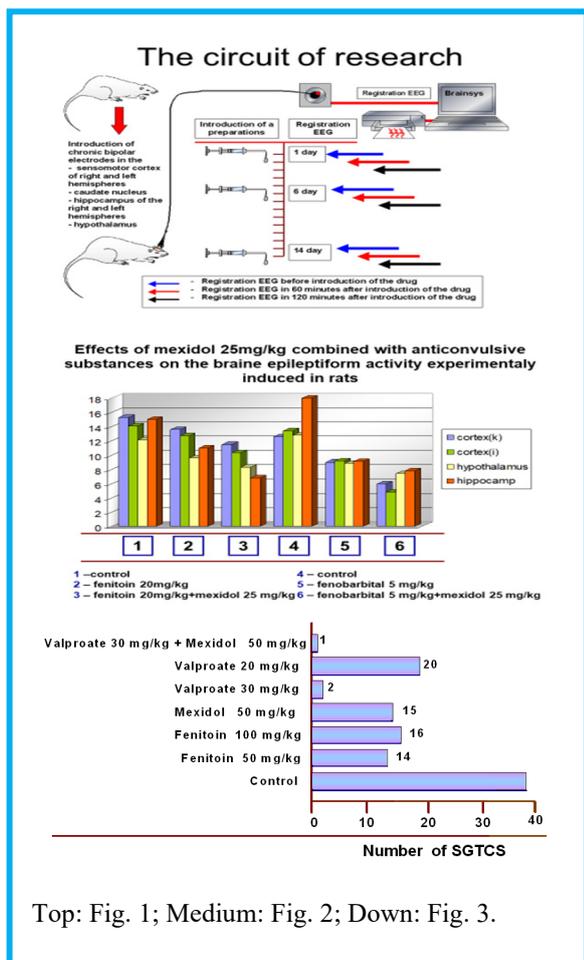
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The aims of modern pharmacotherapy of epilepsy are total suppression of seizures, avoiding adverse events and retaining the patient's social and occupational activity. About 30% of patients with focal epilepsy have hard-to-cure forms which require the use of more than two anticonvulsants in high doses. As a result, a lot of side effects or adverse events have occurred, including decreased levels of wakefulness, attention and memory, which leads to difficulties in learning and professional

activities, as well as disfunction of internal organs (liver, kidney, etc.). The most justified approach to increase the effectiveness and reduce the side effects of anticonvulsants is their combined use with antioxidants and neuroprotectants based on the important role of free-radical processes in the pathogenesis of epilepsy. Ethylmethylhydroxypyridine succinate or Mexidol, which is an antioxidant, antihypoxant and synthesized in Russia, is approved for use in patients with various neurological disorders and is included in the Russia State Registry of Medicines. In Fig. 1, chronic cobalt model in rats with implanted electrodes allowed to trace the formation of epileptic focus in space and time. (Fig. 1 of experimental model). Mexidol was used in combination with phenytoin and phenobarbital (Fig. 2) and valproic acid (Fig. 3). In these cases there was a reduction of epileptic activity in all epileptogenic structures compared to both controls and monotherapy with anticonvulsants ($P>0.05$) (1,2). 36 patients with structural epilepsy who received Depakine Chronosphere at a dose of 1000 to 2000 mg (1 or 2 times daily) with 2 treatment courses of Mexidol per year, and were followed up for 2 years. Comparative clinical and EEG analysis revealed a huge efficacy of the combined use of anticonvulsant (Depakine Chronosphere in a daily dose of 1000, 1500, 2000 mg) with an antioxidant (200 mg of Mexidol, which is 5% solution of 4 ml). Glycine, as a neuroprotective agent, plays a crucial role as neurotransmitters in the central nervous system (3). Under hypoxic conditions, glycine has been observed to improve the lifespan of neurons in the cerebral cortex (4). The use of glycine in clinical practice is promising in terms of reducing the risk of seasonal epilepsy exacerbations.

Key words: epilepsy; anticonvulsants; antioxidant; mexidol.

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Top: Fig. 1; Medium: Fig. 2; Down: Fig. 3.

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Personalized medical and psychological aspects of stress-related disorders in dental specialists

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Currently, due to the introduction of new approaches in the work of a dentist, the problem of improving the quality of work of dental specialists has become urgent. A detailed analysis of the factors that negatively affect the performance of professional functions by a dentist and the most significant factors of the formation of professional stress and the risk of burnout syndrome in this professional group, the features of clinical symptomatology, occupational stress and professional burnout syndrome, the nature of disorders of the nervous systems and other psychophysiological changes caused by professional burnout syndrome involves the development of new approaches to the organization of medical care, providing early detection of symptoms of damage to the nervous system that cause professional burnout syndrome in order to further correct and prevent them in order to extend the professional longevity of workers. Scientific and practical development of a system of measures to improve the quality of work of a dentist, based on the correction of disorders of the nervous system and other psychophysiological changes in this category of specialists. To objectify the data, a diagnostic psychophysiological complex was used, including the following methods. Methods for assessing the state of the vegetative nervous system. The study of the state of the vegetative nervous system was carried out with the analysis of the parameters of heart rate (HR), respiratory rate (RR), blood pressure (BP) (UA-787, A&D Medical, Japan). The measurements were carried out on the brachial arteries on the right and left arms, with the analysis of indicators of the level of heart rate (bpm), systolic blood pressure (SBP), diastolic blood pressure (DBP) and asymmetry of the blood pressure level (mm Hg). Vegetative Kerdo index and Hildebrant coefficient were calculated. These indicators were recorded at rest (initial vegetative tone). To diagnose the syndrome of vegetative dystonia, the "Questionnaire for identifying signs of vegetative changes" was used (Wayne A.M., 1998). Orthostatic tests (Cardiovegetoster, MBN, Moscow, 2005). The study included recording cardio intervals with the calculation of the following parameters: RR, SI, period and power of HRV - HF, period and power of MB1 - LF and MB2 - VLF, SDNN,

RMSSD, pNN50, CV, TP, LF / HF, IARS in the sitting position and in orthostasis. Measurement of systolic blood pressure (SBP) when standing up. The difference in SBP was measured in the prone and standing positions at the third minute of postural modeling. Change in SBP by 30 mm Hg. and below indicates insufficiency of efferent sympathetic vasoconstrictors. Measurement of diastolic blood pressure (DBP) in the isometric tension test (ITT). The patient is squeezing the dynamometer for 3 minutes with a force of 30% of the maximum. Measurement of blood pressure is carried out before and in the third minute of the test. Increase in DBP by 10 mm Hg. and less evidences of the defeat of the efferent sympathetic vasoconstrictors. Psychodiagnostics examination included a set of tests to study the personal characteristics and psychological status of the subjects. The presence of dentist's occupational stress was determined by using the "Scale of Occupational Stress". The Scale of Occupational Stress (Fontana D., 1995) consists of 22 questions and allows you to get an idea of the severity of stress by scoring (the maximum number of points is 60). If the subject scores on a scale of 0 - 15 points, we can assume that he is not in a state of stress, has no signs of emotional stress, and the activity does not cause him any difficulties. At 16 - 30 points, a moderate level of stress is recorded for a busy and hard-working specialist who experiences mental stress. However, they have not had signs of exhaustion of adaptive mechanisms yet. A stress level of 31 - 45 points indicates that stress is a problem and working at this level of stress, the subject may experience significant difficulties in work. The development of neurotic and psychosomatic disorders is also possible. If a stress level of 46-60 points is fixed, then stress will be a significant problem for such a specialist, and it may be close to the stage of exhaustion of the general adaptation syndrome, when professional activity is significantly disrupted. The risk of developing mental and psychosomatic disorders increases sharply. Besides stress assessment, the methodology allows for meaningful analysis to determine the significance of activity parameters in the development of occupational stress. As a result of such an analysis, the following can be distinguished: work stress (maximum score - 5), disruption of contacts in the team (5 points) and with management (5 points), self-esteem level (5 points), violations in personal life (3 points). In addition, the technique allows assessing the representation in the mental state of the subject, neurotic symptoms specific to various types of adjustment disorders (depressive, anxiety, phobic), indicating the degree of stress or exhaustion of adaptive mechanisms. The advantage of the technique is its simplicity and accessibility. To determine the level of professional burnout, the technique "K. Maslach's burnout questionnaire - general version" (Maslach Burnout Inventory - MBI, Maslach C., 1982) was used. It was edited by Vodopyanova M.E. (2008) and

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supplemented by the mathematical model of Bekhterev National Research Medical Center for Psychiatry and Neurology. The questionnaire consists of 22 items, according to them, it is possible to calculate the values of three scales: "Emotional exhaustion" (EE), "Depersonalization" (DP), "Reduction of professional achievements" (PA). Each item is scored on a 7-point scale from 0 (never experience), 1 (several times a year or less) to 5 (several times a week) and 6 (everyday).

"Emotional exhaustion" (maximum score - 54) manifests itself in experiences of reduced emotional tone, increased mental exhaustion and affective lability, loss of interest and positive feelings for others, a feeling of "satiation" with work, dissatisfaction with life in general. In the context of the burnout syndrome, "depersonalization" involves the formation of special, destructive relationships with others. With a total score of 0-15 points on this scale, a low level of emotional exhaustion is diagnosed, 16-24 - medium, over 25 - high.

"Depersonalization" (maximum score - 30) is manifested in emotional detachment and indifference, formal performance of professional duties without personal inclusion and empathy, sometimes in negativism and cynical attitude. At the behavioral level, "depersonalization" manifests itself in arrogant behavior using of professional slang, humor, and labels. With a sum of 0-5 points, a low level of depersonalization is determined, 6-10 - medium, over 11 - high.

"Reduction of professional achievements" (maximum score - 48) reflects the degree of satisfaction of a specialist with himself as a person and as a professional. The unsatisfactory value of this indicator reflects a tendency to a negative assessment of one's competence and productivity and, as a result, a decrease in professional motivation, an increase in negativity in relation to official duties, a tendency to disclaim responsibility, to isolate from others, detachment and non-participation, avoidance of work. The sum of points over 37 indicates a low level of reduction of professional achievements, 31-36 is about the average, 30 or less is about the high level.

The subject, demonstrating high scores on the "emotional exhaustion" and "depersonalization" scales and low scores on the "professional efficiency" scale, has a high degree of burnout. System physiological index dynamics at psychorelaxation correction Cardiovascular, BP, HR, Peripheral vascular resistance, Cardiac output decrement fall decrement, increase breathing, Respiratory rate oxygen intake fall subsidence, Musculoskeletal electrical activity decrement Axion alpha-rhythm (EEG) enhancement, Endocrine, Plasma cortisol, catecholamine. cholesterol decrement.

•Psychological reactions of dentist's occupational stress have their own characteristics: disappointment in the profession, a general negative attitude towards life prospects, a feeling of being unclaimed; at the same time,

a high level of reactive anxiety, dominance of asthenic emotions, reduced indicators characterizing the quality of life are typical, with an increase in the severity of all identified changes, corresponding to an increase in the duration of professional experience.

•The results of the instrumental assessment of the functional state of the autonomic nervous system in the dentist's professional burnout syndrome indicate the occurrence of violations of the adaptive capabilities of the functional systems of the body, while the phenomenon of exhaustion is characteristic, leading to a subsequent overstrain of the adaptive systems of the body. A common characteristic of the psychological status of the majority of patients at a dental appointment (71.2%) is fear and the dominance of signs of negative affectivity, manifested by an average and high level of anxiety; however, patients differ in types of emotional and behavioral responses and can be attributed to different character groups.

Key words: personalized; medical and psychological stress-related disorders, dental specialists.

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Conclusive remarks

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**Arrivederci, Auf Wiedersehen, Au revoir,
Goodbye to 2025Padua Days on Muscle and
Mobility Medicine, February 27 to March 1,
2025 – Thermae of Euganean Hills (Padua), Italy**

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