

**The EJTM Special “Mobility in Elderly”**

This Issue of the European Journal of Translational Myology/Basic Applied Myology Vol. 25 (4), 2015 belongs to the series of *EJTM Specials on “Mobility in Elderly”*. The issue collects reviews and articles. Their contents were presented at the “MOBIL project completion congress” held at the Wilhelminenspital Wien, Austria the November 8, 2014 to discuss results of the Project: *MOBIL (Mobility in Elderly 2008-2014)*, supported by European Regional Development Fund - Cross Border Cooperation Programme Slovakia – Austria 2007–2013 (Interreg-IVa), project *Mobilität im Alter, MOBIL, N\_00033* (partners: Ludwig Boltzmann Institute of Electrical Stimulation and Physical Rehabilitation, Austria, Center for Medical Physics and Biomedical Engineering, Medical University of Vienna, Austria, and Faculty of Physical Education and Sports, Comenius University in Bratislava, Slovakia).

Since many years the Ludwig Boltzmann Institute of Electrical Stimulation and Physical Rehabilitation, directed by one of us (Prof. Helmut Kern) is counting on the collaboration not only of Austrian and Slovakian Colleagues but also of several research teams of other European and Transatlantic countries, as it is witnessed by the Authors of the reviews and articles of this *EJTM Special on “Mobility in Elderly”* and the 150 coauthors of the 50 papers published in international journals listed in PUBMED that the Ludwig Boltzmann Institute of Electrical Stimulation and Physical Rehabilitation, Vienna, Austria published from 2004 to 2015.

From 2000 that a fruitful collaboration led by Prof. Helmut Kern succeeded to be granted by the EU to respond to the needs of a peculiar group of Spinal Cord Injury persons with complete *Conus* and *Cauda Equina* lesion that completely disconnect the leg muscles from their innervating spinal cord motor neurons. If irreversible, the complete lesion results in degeneration of the muscle tissue, if not counteracted by a purpose-developed Functional Electrical Stimulation (FES) strategy designed and developed in Vienna starting from the 1990s. The final evidence of the effectiveness of the Vienna rehabilitation strategy, was collected thanks to the support of the EU Commission Shared Cost Project RISE (Contract no. QLGS-CT-2001-02191) led by Prof. W. Mayr, Dr. C. Hofer (engineering part), Prof. H. Kern (clinical part) with the expert collaboration of C. Forstner, M. Mödlin, M. Vogelauer, S. Löffler, P. Drewniak, H. Stöhr, C. Rossini, S. Zampieri of the LBI, with the partnership of M. Bijak, D. Rafolt, E. Unger, Center of Biomedical Engineering and Physics, Vienna, Austria; H. A. Cerrel Bazo, Neuromotor Rehabilitation, Cernusco, Milan, Italy; M. R. Dimitrijevic, Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, TX, USA; G. Exner, Spinal Cord Injury Center, Hamburg, Germany; E. Gallasch, Physiology, Graz, Austria; H. J. Gerner and R. Rupp, Orthopedics, Heidelberg, Germany; W. Girsch, Orthopedics, Speising, Vienna, Austria; T. Helgason, P. Ingvarsson, S. Yngvason, Landspítali-University Hospital, Reykjavik, Iceland; J. Hufgard, M. Obrovsky, Rehabilitation, Klosterneuburg, Austria; H. P. Jonas, Rehabilitation, Bad Häring, Tirol, Austria; S. Lotta, Villanova sull’Arda (PC), Italy; D. Maier and M. Potulski, Murnau, Spinal Cord Injury, Murnau, Germany and the scientific support of Italian Research Teams led by U. Carraro, University of Padova and F. Protasi, University of Chieti. Prof. S. Salmons and J. Jarvis, Liverpool University were also engaged in animal experiments, mainly performed in rabbit.

The final report of the EU RISE trial, published in 2010 was the happy-end of a long debated basic and clinical topic, which first studies may be found in the literature of the Nineteenth Century,<sup>1</sup> though it was in the 1940s that the study of events occurring in denervated muscle fibers emerged as a topic distinct from the more clinical relevant studies of nerve regeneration and muscle reinnervation.<sup>2-4</sup> During the following twenty years, the reports increased in numbers year after year. Finally in 1962 the book edited by Ernest Gutmann summarized previous knowledge from biology to rehabilitation by electrical stimulation and opened the modern era of “*The Denervated Muscle*”.<sup>5</sup>

Three pioneers of the modern studies on muscle denervation contributed to the 2014 EJTM Special on “*The Long-Term Denervated Muscle*” and/or lectured at the 2014Spring PaduaMuscleDays: 1. Bruce M. Carlson, co-author of several papers with Ernest Gutmann on regeneration of transplanted muscles, opens the EJTM Special with the review “*The biology of long-term denervated skeletal muscle*”.<sup>6</sup> He offers to researchers the basic concepts and the results to understand problems and actual or future solutions that continue to nurture Translational Myology; 2. Terje Lømo was the first in 1972 to electrically stimulate denervated rat muscle to test the hypothesis that induced activity modifies muscle properties and indeed he demonstrated that it suppresses one of the hallmarks of muscle fiber denervation, i.e., ACh sensitivity spreading from the synaptic area to the whole sarcolemma.<sup>7</sup> Prior to 1972, it was believed that neurotrophic factors, not related to excitatory impulse transmission, played a role in spontaneous fibrillation, another functional marker of muscle denervation, whose appearance is inversely related to the length of the degenerating nerve stump. Lømo and co-workers demonstrated, instead, that chronic electrical stimulation of denervated rat muscles caused ACh-sensitivity to disappear from denervated muscles already ACh supersensitive. Further, he showed that the passive electrical properties and the contractile characteristics that distinguish fast and slow fiber types are under the control of the patterns of activity.<sup>8,9</sup> In a report at the First Abano Terme Meeting on Rehabilitation (1985), there reprinted,<sup>10</sup> Lømo et al. defended the hypothesis against the criticisms of authoritative neuroscientists. In his 2014 Commentary,<sup>11</sup> he states “*While reports favoring the existence of neurotrophic factors were numerous before 2000, they have now essentially disappeared from the literature, including original research papers, textbooks and handbooks, which suggest that the hypothesis is no longer arguable. Thus, the results that I presented in our paper in 1985 seem to have held up rather well*”. We hope that the EJTM Special on long term denervated muscle, rising again the interest of clinicians and scientists (Terje Lømo, included) on rehabilitation of denervated muscle may add to his merits the pioneering evidence that activity, anyhow imposed, strongly modulate trophism and characteristics of denervated muscles; 3. Clara Franzini-Armstrong lectured at the 2014Spring PaduaMuscleDays on “*Structure-function relationships in skeletal muscles. Lessons from ultrastructure*”.<sup>13</sup> She remembered to us that “*Muscle fibers have a stereotyped organization of contractile myofibrils and membrane*

systems best defined by their ultrastructure. The sliding filament model (in 1945) established currently accepted principles of most cell motility”. Her many contributions to the study of the muscle membrane systems and ability to attract young brilliant scientists to electron microscopy are well known and demonstrated also by two speakers of the 2014Spring PaduaMuscleDays, Feliciano Protasi and Simona Boncompagni of Chieti University.<sup>14,15</sup> They have been and are strongly contributing to the success of FES for permanently denervated muscles.<sup>16</sup> We would like to add to Clara’s many merits, the pioneering electron microscopy study in the field of muscle denervation: her 1963 article “An electron microscope study of denervation atrophy in red and white skeletal muscle fibers”.<sup>17</sup>

Standing on the shoulders of these giants, two of us contributed to the EJTM Special three articles that describe history and results of an application of the concepts and discoveries of Bruce M. Carlson, Terje Lømo and Clara Franzini-Armstrong, namely the Vienna Rehabilitation Strategy by home-based Functional Electrical Stimulation (h-b FES) for permanently denervated muscles (Kern H, Carraro U. “Home-based Functional Electrical Stimulation for long-term denervated human muscle: History, basics, results and perspectives of the Vienna Rehabilitation Strategy”).<sup>18</sup> Analytical tools and devices, designed and implemented to diagnose, treat and follow up the *Conus Cauda* complete syndrome that paralyze large muscles of human legs are also described.<sup>18</sup> Among the new analytical tools, Gargiulo P, Helgason T, Ramon C, Jónsson H jr, Carraro U describes “CT and MRI assessment and characterization using segmentation and 3D modeling techniques: applications to muscle, bone and brain”.<sup>19</sup> Recently, a multi-disciplinary team of the Interdepartmental Research Center of Myology of the University of Padua is applying the Vienna principles to the apparently easier cases of peripheral incomplete denervation of limbs. To support the project, denervated muscle fibrillation analyses are revisited in the article of Pond A, Marcante A, Zanato R, Martino L, Stramare R, Vindigni V, Zampieri S, Kern H, Masiero S, Piccione F “History, mechanisms and clinical value of fibrillation analyses in muscle denervation and reinnervation by Single Fiber Electromyography and Dynamic Echomyography”.<sup>20</sup> Further, in collaboration with his international partners, Dr. Kern is extending the benefits of h-b FES to those subjects, which for different reasons suffer the consequences of muscle weakness, from the mild but unrelenting process of aging,<sup>21-24</sup> to the devastating fast progression of muscle cachexia in cancer patients.<sup>25,26</sup>

The present 25 (4), 2015 EJTM Special “Mobility in Elderly” is dedicated to the results of his recent studies, in particular to the Aging Topic. Supported by European Regional Development Fund - Cross Border Cooperation Programme Slovakia – Austria 2007–2013 (Interreg-Iva), project Mobilität im Alter, MOBIL, N\_00033the International group of Prof. Helmut Kern collaborators have produced remarkable results published in International impacted journals that are listed below. Here we would like to list and thanks all the 150 authors of the 50 papers in international journals listed in PUBMED that the Ludwig Boltzmann Institute of Electrical Stimulation and Physical Rehabilitation, Vienna, Austria published from 2004 to 2015.<sup>27-76</sup>

Without their strenuous scientific, translational and clinical work and brilliant intellectual contributions nothing would have been achieved: Abruzzo PM, Adami N, Ambrosio F, Ashley Z, Baraibar MA, Barberi L, Bassetto F, Belia S, Bijak M, Bily W, Biral D, Blaauw B, Boato N, Boncompagni S, Bosco G, Bottinelli R, Burggraf S, Canepari M, Carnio S, Carraro U, Coletto L, Corbianco S, Cvecka J, Danieli-Betto D, Danner SM, De Rossi M, di Tullio S, Dimitrijevic MR, Doria A, Fanó G, Fend M, Ferrero M, Forstner C, Francini F, Franz C, Friguet B, Fruhmant H, Fulle S, Gallasch E, Gargiulo P, Gava P, Germinario E, Ghirardello A, Gobbo V, Grim-Stieger M, Gudmundsdóttir V, Haller M, Hamar D, Haslinger W, Helgason B, Helgason T, Hendling M, Hoellwarth U, Hofer Ch, Hofstoetter US, Ingvarsson P, Jäger H, Jarvis JC, Jernej R, Kaider A, Kern H, Khan MM, Kinz G, Knútsdóttir S, Kovarik J, Krenn M, La Rovere R, Lanmuller H, Lapalombella R, Lenaz G, Li F, Löfler S, Longa E, LoVerso F, Maffei M, Mancinelli R, Mandl T, Marcante A, Marchionni C, Marini M, Masiero S, Mayr W, McKay WB, Merigliano S, Meyerspeer M, Mildner E, Minassian K, Mödlin M, Moser E, Mosole S, Müller L, Musarò A, Nejc S, Nori A, Paolini C, Paternostro-Sluga T, Pelosi L, Persy I, Piccione F, Pietrangelo L, Pietrangelo T, Pinter MM, Podhorska-Okolow M, Pond A, Protasi F, Rafolt D, Rakos M, Rampudda ME, Raschka D, Raschner C, Rattay F, Ravara B, Reichel M, Reischl M, Reynisson PJ, Richter W, Romanello V, Rosker J, Rossini K, Rudolf R, Rupp R, Salmons S, Sandri M, Sarabon N, Sarzo G, Sbardella S, Schils S, Scordari A, Sedliak M, Sgarbi G, Squecco R, Stramare R, Strohhofner M, Sutherland H, Tansey KE, Tirpakova V, Trimmel L, Unger E, Valente M, Vatsndal B, Vecchiato M, Vindigni V, Vogelauer M, Yngvason S, Zampieri S, Zanato R, Zanin ME.

Finally, the conclusive remarks of Prof. Helmut Kern at the 2014 Vienna MOBIL project completion conference: *I think the presentations were fantastic and they showed that we have done a lot of work in the past 4 years. Every topic here is special and helping our goal: keeping seniors more mobile and prevent them from falling. This may even be the main task for the future. How to train, measure and correlate the outcomes are the most important things. Further, it is very important that when we stimulate we will not avoid the nerve regeneration process. We need precise training procedures. Prof. Hamar’s collaborators are the specialists to work this out. We look forward to our future collaboration and our next project (and preparation of a grant proposal) will start immediately after this conference. One thing only I left to say, thanks to all, and in particular to Mike Willand, whose travel from home to Vienna was the longest.*

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