FES in Europe and Beyond: Current Translational Research

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Abstract

Capacity of adult neural and muscle tissues to respond to external Electrical Stimulation (ES) is the biological basis for the development and implementation of mobility impairment physiotherapy protocols and of related assistive technologies, e.g. Functional Electrical Stimulation (FES). All body tissues, however, respond to electrical stimulation and, indeed, the most successful application of FES is electrical stimulation of the heart to revert or limit effects of arrhythmias (Pace-makers and Defibrillators). Here, we list and discuss results of FES current research activities, in particular those presented at 2016 Meetings: the PaduaMuscleDays, the Italian Institute of Myology Meeting, the 20th International Functional Electrical Stimulation Society (IFESS) conference held in Montpellier and the Vienna Workshop on FES. Several papers were recently e-published in the European Journal of Translational Myology as reports of meeting presentations. All the events and publications clearly show that FES research in Europe and beyond is alive and promises translation of results into clinical management of a very large population of persons with deficiencies.

Key Words: FES, denervated muscle, mobility impairment, aging, prevention and assistive technology, rehabilitation, biomedical technology

Ability of neural and muscle tissues to respond to external Electrical Stimulation (ES) is the sound biological basis of established therapeutic managements of mobility impairments, assistive technology and of the current research activities aimed to extend its clinical applications. All the body tissues, however, respond to ES and, indeed, the most successful application of Functional Electrical Stimulation (FES), though known under other names or acronyms, is the electrical stimulation of the heart to revert or limit effects of arrhythmias (Pace-makers and Defibrillators). We would like to list and discuss here results of current research activities on FES, in particular those published in the European Journal of Translational Myology after presentation during the 2015 XI Meeting of the Italian Institute of Myology (IIM), the 2016 Spring PaduaMuscleDays, the 2016 Vienna FES Workshop and the 2016 International Conference of IFESS society held in Montpellier France.

In Table 1 are listed the subtopics of FES research and applications published in the European Journal of Translational Myology that will be discussed in the following sections. They are only some of a much longer list that represent the many subtopics of FES, i.e., i) Biological bases of FES for Neuromuscular Mobility Impairments; ii) FES for Arm, Leg and Body Motility; iii) FES for Swallowing, Micturition, Gastric function restoration; iv) FES as a countermeasure of muscle weakness and atrophy; v) FES and mechanical devices (wearable robots, cycles...); vi) FES for Pain Management; vii) Sensor interfaces to control FES (BCI, EMG, IMUand more); viii) FES advanced technology to improve efficiency and selectivity.

2015 XI Meeting of IIM, Italy and 2016 Spring PaduaMuscleDays

Among other scientific topics, during the 2015 IIM meeting the molecular mechanisms of muscle atrophy, wasting and diseases were deeply discussed. One of the remarkable features of skeletal muscle is, indeed, the capacity to adapt its morphological, biochemical, and molecular properties in response to several events.
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Exercise, attenuates the functional decline associated with aging, improving muscle strength and mass, maintaining the overall size of muscle fibers (decreasing during aging), activating satellite cells and guaranteeing muscle adaption. Based on several evidences, we can also speculate that FES mimics the effects of endurance training, since they do not induce muscle damage, and activate comparable molecular networks.

Many of these mechanisms were discussed in recent papers published in the European Journal of Translational Myology and during the 2016 Spring PaduaMuscleDays as the main determinants of the positive effects of physical exercise and FES when applied to therapeutic and rehabilitation strategies aimed to prevent or revert the consequences of aging and mobility impairments.

### 20th Conference of the International Functional Electrical Stimulation Society, IFESS - 2016

The International Functional Electrical Stimulation Society (IFESS) is an inter-professional and collaborative organization, whose main objective is promotion of research, applications and understanding of electrical stimulation as it is utilized in the field of medicine.

The theme of the 20th IFESS conference, organized in Montpellier, France in 2016 by INRIA institute and Montpellier university was «Hybrid Approaches of IFESS». The idea being to highlight ongoing research activities associating FES to other assistive approaches such as exoskeletons or central nervous system (CNS) stimulation. The notion of hybridity can also be seen from the perspective of the multidisciplinary face of the field. Three special sessions were dedicated specifically to this theme with articles associating FES to 1) wearable robotics, 2) CNS stimulation and 3) cycling devices. Electrical stimulation can be applied in a large panel of situations and some of the emerging applications have been presented in the special session: “Emerging FES interventions, with original and promising studies”. Electrical stimulation activates both efferent and afferent pathways. This property is extremely appealing in the context of functional rehabilitation and neurological recovery. The engagement of patients is mandatory to increase the potential of the training. This was the object of the special session “FES and fun” which explores different approaches to motivate the patients to actively participate into their rehabilitation protocol. In the regular sessions, articles insisted in the recent advances in technology to improve stimulation efficiency and selectivity, to explore new modalities and applications of FES. Engineers and Clinicians demonstrated in their articles the importance and potential of this very active research field. We wish to thank all authors of the articles that have contributed to EJTM (Tables 2 to 7) and for making the EJtm Special Section on 2016 IFESS Conference an exciting and intriguing read.

### Table 1: List of subtopics of Functional Electrical Stimulation research and management

1. Biological bases of FES for neuromuscular mobility impairments
2. FES for upper and lower body mobility
3. FES for swallowing, micturition, gastric and other vital functions
4. FES as a countermeasure of muscle atrophy, weakness and aging
5. FES combined with mechanical devices (wearable robots, cycles and more ...)

However, under pathological conditions skeletal muscle loses its adaptability, leading to atrophy and wasting. The continual synthesis and degradation of cell proteins is the result of normal intracellular metabolism and represents an important homeostatic function of muscle tissue. Muscle wasting, in contrast, is a process in which the delicate balance between anabolic and catabolic processes is impaired. In recent years, age-related diseases and disabilities have become of major interest and importance for health. The pathological process associated with aging is known as sarcopenia, characterized by a progressive loss of mobility and a decrease of the life quality. Society at large will benefit from delaying, as much as possible, the sarcopenia economic and social consequences. In elderly, muscles become atrophic (loss in muscle mass) and weaker (loss in muscle force), more susceptible to damage and consequently regenerate and recover more slowly than in younger individuals.

During the IIM-Myology meeting, several signaling pathways have been discussed as key maintenance regulators of muscle mass or triggers of muscle wasting. Nevertheless, despite the new discoveries in this field, no effective therapies are still available. Therefore, it is of fundamental importance to gain greater knowledge about the cellular and molecular processes controlling this debilitating condition to find effective countermeasures. FES is one of the approaches that attracted much attention in the last 10 years, based on practical considerations: i) ES can be applied to people that cannot carry out normal physical activity; ii) it modulates similar factors associated with physical exercise; iii) it improves muscle mass and function in sedentary elderly people. In particular, it has been demonstrated that ES activates, at the level of skeletal muscle, the growth factor IGF-1, which in turn promotes anabolic pathways increasing protein synthesis while reducing protein degradation. IGF-1 and FES appear to be responsible for the increase in muscle performance. Interestingly, ES, similarly to physical exercise, attenuates the functional decline associated with aging, improving muscle strength and mass, maintaining the overall size of muscle fibers (decreasing during aging), activating satellite cells and guaranteeing muscle adaption.
Table 2. European Journal of Translational Myology, 2016. FES papers: Subtopic 1. Biological bases of FES for neuromuscular mobility impairments

| Review | Carraro U, Kern H. Severely atrophic human muscle fibers with nuclear misplacement survive many years of permanent denervation. Eur J Transl Myol 2016;26:76-80.15 |

12th Vienna International Workshop on FES, September 8th-9th, 2016

The "Vienna Workshop on Functional Electrical Stimulation" was held the first time in 1983 in Vienna, Austria. Since then it is organized by the Center for Medical Physics and Biomedical Engineering (former: Center for Biomedical Engineering and Physics), the Medical University of Vienna and the Austrian Society for Biomedical Engineering every three years in Vienna or locations close to Vienna. This scientific conference provides a platform for researchers to present and discuss their recent work whilst visitors can expect a representative and actual overview of the state of the art of FES. Traditionally, parallel sessions are avoided. Since the 10th Workshop (2010) all conference proceedings are available on DVD: “30 years of FES history on one click” (http://fesworkshop.org).

This year’s Workshop was held at the renovated Campus of the Medical University Vienna, a place with a long history in medical research.

The conference started with two Pre-Conference Courses "FES of Denervated Muscles – An Essential Therapeutic Option after Peripheral Nerve Lesion" (Organizers: Mayr W., Krenn M., Biowski P., all from Vienna, Austria) and "Non invasive posterior root stimulation for assessment and modulation of spasticity and motor control" (Organizers: Mayr W., Krenn M., both Vienna, Austria and Dimitrijevic M., Houston, TX, USA) designed as hands-on workshops with a comprehensive introduction on physiological, clinical and technical basics, safety issues, handling of equipment, guidelines and protocols.

As FES of denervated muscles differs fundamentally from classical neuromuscular ES, the main particularities were addressed in an open interactive discussion, scientifically based on the strong clinical, functional and structural results of the EU Program RISE.6-8
The goal was to train qualified medical staff to a level that allows confident, safe and efficient clinical application of the introduced methods.

The scientific program started with two special topics on Functional Rejuvenation in Aging and Electrical Stimulation in Neuromuscular Disorders. Then it continued with a special session where the outcomes of the EU project RETRAINER (http://www.retrainer.eu/) were introduced with enough time to get in touch with the project leaders and to try out first prototypes for robotic supported reaching and grasping training.
The following sessions covered findings in Basic Research, Neuromodulation, Rehabilitation strategies, FES Exercise and in the more hardware oriented part Technologies, Engineering, Sensors.

Three excellent keynote speakers provided insight into latest findings in FES and neighboring fields.

Jarvis J. (Liverpool, GB) introduced the potential of genomics, metabolomics and proteomics technologies to better understand cell biology in his talk "Neuromuscular cell biology and "omic technologies". Lukanočič A. (Ljubljana, Slovenia) discussed "Neuromodulation in the treatment of pelvic floor dysfunctions" and Podesser B. (Vienna, Austria) talked about "Animal research in FES" and the related possibilities and regulations.

Details of the program of the 12th Vienna International Workshop on FES, September 8th-9th, 2016 are available at the link: http://2016.fesworkshop.org/

Conclusions
Altogether, evidence demonstrates that FES basic, translational and clinical research in Europe and beyond is alive. Translation of results to clinical therapies for a large population of patients is much more than a hope.

Author’s contributions
All authors equally organized the draft and wrote the typescript.

Table 4. European Journal of Translational Myology, 2016. FES papers of Subtopic 3. Arm motility

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Table 5. European Journal of Translational Myology, 2016. FES papers: Subtopic 3. FES for swallowing, and other applications

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Table 7. European Journal of Translational Myology, 2016. FES papers of Subtopic 6. FES Technology

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<td>Laursen CB, Nielsen JF, Andersen OK, Spaich EG. Feasibility of using Lokomat combined with functional electrical stimulation for the rehabilitation of foot drop. Eur J Transl Myol 2016;26:268-73.64</td>
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Conflict of Interest
The authors declare no potential conflict of interests.

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