Galvani’s delayed legacy: neuromuscular electrical stimulation

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The medical device industry has grown accustomed to the frustratingly long path to successful commercialization of clinical technologies. However, the use of electrical stimulation to treat paralyzed muscles must be a record. Bioelectricity was first discovered by Luigi Galvani circa in 1770 when he made a frog muscle twitch by inadvertently creating a battery from surgical instruments made of dissimilar metals [1]. Combine that discovery with the compelling needs of millions of patients suffering from strokes, spinal cord injuries and so on, and one might expect neuromuscular electrical stimulation to be standard treatment. It is not. The problem certainly is not inherent cost; consider the consumer electronics industry, which provides comparable electronic sophistication in children’s toys. It is not lack of biomedical sophistication; consider the success of cochlear implants in virtually eliminating sensorineural deafness [2].

Certainly there have been many successful applications of neuromuscular electrical stimulation [3-9]. Several companies manufacture transcutaneous electrical stimulation units that produce output pulses strong enough to excite underlying muscles; some clinics prescribe these occasionally for patients. However, few patients appear sufficiently motivated to accept the unpleasant skin sensations and the hassle of applying electrodes and adjusting stimulation parameters. The field certainly was not helped by infomercials (now banned) claiming weight-loss and body-building benefits.

More specific and selective control of muscles without adverse sensation can be achieved by implanting the stimulating electrodes in the muscles themselves. Percutaneous wires can be used for short-term stimulation, although most clinical conditions that could benefit are chronic [7,8]. An ambitious commercial product involving a fully implanted multichannel stimulator (FreeHand™, NeuroControl Corp. [9]) was withdrawn because its clinical benefit (assisted grasp in quadriplegic patients) did not justify the expense and invasiveness of its surgical implantation. A novel technology for injectable, wireless intramuscular microstimulators has been in clinical trials for several years (BIONs™ [10,11]) but has yet to evolve into a commercial product.

It may be time to dust off Galvani’s legacy and put it to work clinically and commercially. We can take advantage of two centuries’ worth of useful lessons:
Neuromuscular stimulation is really neural stimulation
The biophysical basis of electrical stimulation is very well understood. Given easily obtained anatomical data, it is relatively simple to construct a mathematical model that accurately predicts absolute and relative effects of various stimulus waveforms from a given electrode design and placement [12]. One might never guess this from the clinical literature, whose methods are rarely presented in a useful way and are often irrational and even self-defeating. Electrical stimulation is not magic. Empirical clinical observations can be understood and improved by the systematic application of science and technology. It is time for clinicians, engineers and neurophysiologists to work together.

Much of the morbidity of paralytic diseases is secondary to muscle disuse, not the paralysis itself
This field started with the goal of making paraplegics walk. That turns out to be difficult, hazardous, and probably of marginal value for reimbursement given well-evolved and highly efficient alternatives such as wheelchairs. Paralyzed patients and their therapists actually prioritize other goals that are both more tractable technically and more important clinically: bowel and bladder function, pressure sores, joint pain, cardiorespiratory function, venous stasis, spasticity and so on [13,101]. These functional problems affect many more patients and consume far more healthcare resources than the loss of limb function that tends to attract our notice. Paradoxically, prevention and treatment of these sequelae is likely to require simpler, less expensive and less invasive technology than making paraplegics walk, but we will not know this until researchers and companies begin investing significant resources in the most significant problems.

Disused muscles undergo substantial but reversible atrophy
Within just a few weeks without activation, muscle fibers have already suffered a substantial loss of contractile myofilaments and a profound change in the physiologic properties of all types of muscle fibers [14]. Most obviously, they produce much less force and all fiber types fatigue very rapidly (within seconds). If the inactive muscles have been kept in a shortened or lengthened position (for example, due to imbalance in residual tone), then there will be substantial loss or addition of series sarcomeres, shifting the force-length relationship for both active and passive tension. In the extreme, a functional system of antagonist muscle pairs is replaced with a useless limb deformed by fixed contractures. While it remains unclear whether sufficient technology exists to produce direct, functional reanimation of a completely paralyzed limb, it has long been known that neuromuscular electrical stimulation can prevent and reverse the effects of disuse atrophy [15,16].

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The central nervous system responds to patterns of use & disuse with substantial plastic reorganization
The fixed and limited functionality implied by the cartoon homunculus inhabiting the sensorimotor cortex is now known to be incorrect. Large shifts in both sensory and motor representations can occur in adults, particularly as a result of intensive use and rehabilitation [17]. However, a limb that is atrophic, contractured, painful or otherwise dysfunctional is likely to preclude such retraining of the central nervous system. Physical therapy and neuromuscular stimulation are complementary, not competitive. The true value of new technologies for neuromuscular stimulation will not be apparent unless, and until, clinical studies exploit this synergy. Unfortunately, the statisticians who design clinical studies and the regulators who approve them tend to prefer simplistic comparative studies.

As a result of several notable commercial successes (deep brain stimulation for Parkinson’s disease, cochlear implants for deafness and spinal cord stimulation for chronic pain), neurostimulation is now hot. Neuromuscular stimulation can take advantage of this historic opportunity to redeem its original promise. The science and the technology are ready. All we need is the discipline to focus collectively on real problems and real opportunities.

References
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