TECHNIQUES AND PROCEDURES

Magnetic Stimulation of the Quadriceps: Analysis of 2 Stimulators Used for Diagnostic and Therapeutic Applications

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Compromised muscle function can be evaluated in respiratory disease patients by supramaximal magnetic stimulation (isometric twitch) of the quadriceps, a technique that is reproducible and objective. We validated the technique, comparing a device used in our laboratory with another reference electromagnet. We also assessed whether the technique could potentially be used to train the muscle by repetitive stimulation.

The Medtronic Magpro (MED) device with a circular coil and the Magstim 200 device (MAG) with a figure-of-eight coil (reference device) were used to stimulate the femoral nerve of 6 volunteers at different percentages of maximal output. MED stimulation was also applied on the quadriceps muscle. We measured voluntary contractions, comparing measurements from the 2 devices and on different days. The stimulation achieved with MED was lower than with MAG, showed greater day-to-day variability, and was not clearly supramaximal. MED quadriceps stimulation was 80.7% of MAG stimulation.

In conclusion, supramaximal stimulation of the quadriceps cannot be guaranteed with MED and the circular coil. However, this device generates sufficient contraction when applied to the muscle to be used for repetitive stimulation.

Key words: *Skeletal muscles. Quadriceps. Femoral nerve. Chronic obstructive pulmonary disease (COPD). Neuromuscular disease Neurophysiology. Lung function tests. Electromagnetism. Magnetic stimulation.*

Estimulación magnética del cuádriceps. Análisis de 2 estimuladores de uso diagnóstico y terapéutico

La estimulación supramáxima o *twitch* magnético isométrico del cuádriceps es una técnica reproducible y objetiva que nos informa sobre la función muscular, que se encuentra comprometida en las enfermedades respiratorias. Hemos validado la técnica estándar y comparado un equipo utilizado en nuestro laboratorio con otro electroimán de referencia. También evaluamos el potencial de la técnica para entrenamiento muscular mediante estimulación repetitiva.

Los equipos Magstim 200 con pala en mariposa (MAG, equipo de referencia) y Medtronic Magpro con pala circular (MED) se aplicaron sobre el nervio femoral de 6 voluntarios, a diferentes porcentajes del estímulo máximo. El MED se aplicó también sobre el músculo cuádriceps (MED-Q). Se realizaron medidas voluntarias y comparaciones entre equipos y días diferentes. El MED alcanzó valores menores que el MAG, con mayor variabilidad entre días y sin clara supramaximalidad. La estimulación MED-Q fue equivalente al 80,7% del MAG.

En conclusión, no puede garantizarse un estímulo supramáximo del cuádriceps con el MED y pala redonda, aunque ésta, aplicada sobre el músculo, genera una contracción que avala este abordaje para la estimulación repetitiva.

Palabras clave: *Músculos esqueléticos. Cuádriceps. Nervio femoral. EPOC. Enfermedad neuromuscular. Neurofisiología. Pruebas de función respiratoria. Electromagnetismo. Estimulación magnética.*

Introduction

In the past, the study of striated muscle of patients with chronic obstructive pulmonary disease (COPD) focused on respiratory muscle function and diaphragm function in particular. However, our interest has progressively broadened and we now also aim to understand "systemic" aspects of the disease. Peripheral muscle function correlates with measures of COPD severity such as the BODE index defined by body mass index, airflow obstruction, dyspnea, and exercise capacity.[1] This index has greater prognostic
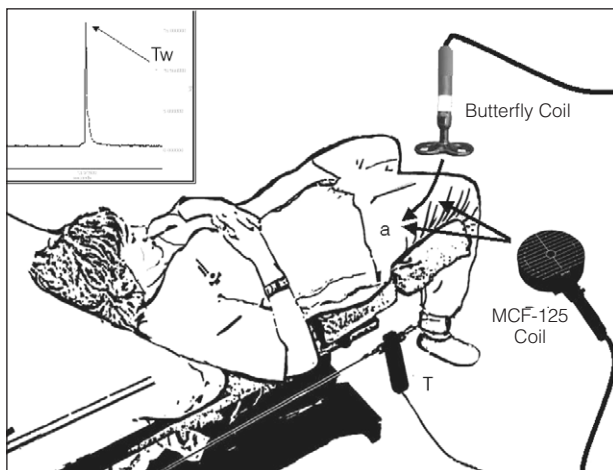
Figure 1. Volunteer prepared to receive a stimulus to the femoral nerve. A transducer (T) connected to the ankle records the force generated. The upper inset shows a sample recording of force after twitch stimulation. The peak value corresponds to the twitch value (Tw). The 2 types of stimulation coils represented correspond to the figure-of-eight or butterfly coil of the Magstim device, which is applied vertically, and the MCF-125 circular coil of the Medtronic device. Stimuli from both coils were applied to the femoral nerve in the inguinal area (*a*) and, in the case of the circular coil, directly to the quadriceps (*b*) in the thigh.

value than obstruction itself, because muscle function is related to exercise capacity[2] and is essentially determined by fat-free mass—a nutritional index of greater prognostic relevance than body mass index.[3]

In patients with COPD, the skeletal muscles affected include the inspiratory muscles themselves, which can be trained to improve function,[4,5] and—above all—leg muscles. Quadriceps function in particular has been widely studied in COPD.[6,7] In this muscle, the characteristics most often observed are loss of type I fibers[8] and lower oxidative capacity.[9,10] These characteristics have been associated with a lower quality of life,[11] lower exercise capacity, and greater health resource use.[12] From the clinical point of view, it is noteworthy that the exercise capacity of many patients with COPD is limited by muscle fatigability rather than dyspnea, even though the respiratory function of these patients is severely impaired.[13]

A technique increasingly used to study peripheral muscle function is measurement of the force exerted by a muscle after supramaximal magnetic stimulation—known as twitch stimulation.[14] In the case of the quadriceps, the procedure described by Polkey et al[15] is usually followed. Quadriceps measurements are widely used in studies of muscle function of patients with COPD given that these muscles are representative of an essential muscle group in the lower limbs.[16] The advantage of this technique is that it is painless, supramaximal—and therefore reproducible—, and can be used as a reliable measure of muscle dysfunction in uncooperative individuals, children, those with central nervous system disorders, and patients in intensive care units or simply in patients with diseases such as COPD,[15] in whom voluntary maneuvers can lead to a much wider spread of results than in healthy subjects.[15,17] The clinical validity

might therefore be questioned, particularly if patients follow training protocols that involve a learning effect. Given that an involuntary test is available that can also detect muscle fatigue,[6,15,16] and the relative ease with which biopsy samples can be taken from the quadriceps, morphological and functional studies could be done that extend our knowledge of the effects of rehabilitation and other interventions on systemic aspects of this disease.

In our study, we aimed to assess the Medtronic Magpro device (MED) with a refrigerated MCF-125 circular coil, which has a broad potential use for diagnosis and also for muscle rehabilitation given that it can apply repeated stimuli over long periods. We wished to determine, on the one hand, the diagnostic yield for measurements with supramaximal stimulation, that is, twitch stimulation of the quadriceps compared to the reference technique,[15] and on the other, the response after directly stimulating the muscle with the coil. Direct application will probably be the most appropriate method for repetitive stimulation of the quadriceps, on which future training programs will be based because it is simple and well tolerated.[18] If we can show extensive muscle activation with a good contractile response, we would expect more efficient training with repeated stimuli than with other therapeutic techniques such as electrical stimulation.[19-21] We can use this training method in patients who, in view of the severity of their disease, would be unable to participate in a conventional respiratory rehabilitation program.[22]

Methods

Description of the Technique

Measurements with twitch stimulation of the quadriceps were made as described by Polkey et al[15] using similar equipment. For 20 minutes before the maneuvers, the volunteers lay on a specifically arranged bed with knees bent at a 90° angle to avoid potentiation of muscle response associated with recent activity. The ankle of the dominant leg was connected to a Biopac tension dynamometer by a nonelastic strap, (Biopac TSD 121C, Biopac Systems, Goleta, California, USA) arranged in parallel to the direction of foot movement. In our study, the signal was amplified with a Biopac system (Biopac Systems), transmitted to a PC, and processed with the AcqKnowledge version 3.7.3 software system for Microsoft Windows (Biopac Systems). Figure 1 shows the position of the patient for stimulation, the coils used, and an example of the twitch signal obtained.

Procedures

Six healthy volunteers (aged between 27 and 50 years old, 3 women and 3 men) were studied for validation of the technique and for assessment of the alternative MED device; the table presents their general and anthropometric characteristics. All of the volunteers had some sort of connection with our lung function testing laboratory but none had been involved with measurements with twitch stimulation of the quadriceps before.

Devices and Application Sites

A Magstim 200 Mono Pulse electromagnet (MAG) (Magstim Co Ltd, Spring Gardens Whitland, Carmarthenshire, Wales, UK) was used. This device was connected to a double 45-mm figure-
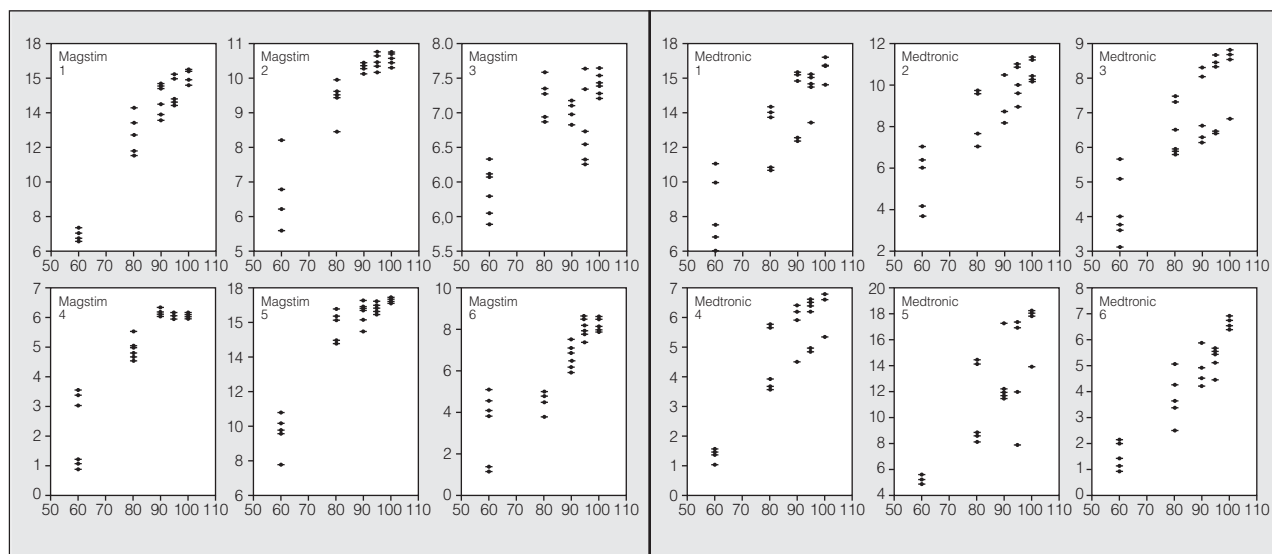
Figure 2. Plots of responses to twitch stimuli with the Magstim device (left) and the Medtronic device (right) in the 6 volunteers studied. With the Magstim device, all volunteers reached a ceiling response: such a response was only observed in volunteers 4 and 5 in the case of stimulation with the Medtronic device.

of-eight (butterfly) coil with a "branding iron" arrangement. The commercial equipment had been modified to generate a field of 2.5 T. The MED readings were taken with the Medtronic Magpro device (Medtronic Denmark A/S, Copenhagen, Denmark) connected to a refrigerated MCF-125 circular coil of 60 mm radius (Figure 1).

Femoral application. The femoral artery was located in the femoral triangle by palpation and the maximum field of the coil was placed below and just to the side of the inguinal ligament. The maximum field was located at the point where the 2 spools of the figure-of-eight coil join (MAG) or in the peripheral area for the circular coil (MED). The positioning was shifted to find the best point and slight adjustments were made to the coil axis while monitoring the response to twitches of equal strength. A series of readings were then taken with 5 twitches at 60%, 80%, 90%, 95%, and 100% of the maximum output in random order. Stimuli were separated by at least 20 seconds to avoid potentiation.[14]

Crural application. For MED measurement of quadriceps response (MED-Q), we directly stimulated the vastus lateralis muscle of the quadriceps muscle group with the MED coil. Stimulation was preferably applied midway between the upper

third and the lower 2 thirds of the body of the muscle, at the point of maximum response. Readings were taken according to the protocol described above.

Supramaximal stimulation. In theory, to measure isometric force generated by twitch stimulation of the quadriceps, stimulation should be supramaximal.[14,15] A stimulus can be shown to be supramaximal by electrophysiological readings or by the presence of a plateau in the stimulus–response curve at stronger stimuli (Figure 2).

Maximal voluntary contraction. Using the same experimental set-up (Figure 1) and the dynamometer with the Biopac system, we measured the maximum voluntary contraction after 5 maximal efforts of isometric contraction with the volunteer in the same position as described earlier (supine position with the knees bent to 90°). These measurements were always made after the MAG, MED and MED-Q readings had been taken.

Repetitions. In all cases, we repeated the magnetic stimulation readings on 2 different days but with the same operator, the same procedure, and ruling out any unusual physical activity on the measurement day or the preceding day.

Anthropometric Characteristics of Study Volunteers, Maximum Voluntary Contraction (MVC), Maximum Twitch Value With the Magstim Device (Tw_{max}), Mean Twitch Values at 100% Stimulation With the Magstim Device (MAG) and the Medtronic Device (MED), and Values for Quadriceps Stimulation With the Medtronic Device (MED-Q)

| Volunteer	Sex	Age, y	Height, cm	Weight, kg	MCV	Tw_{max}	MAG	MED	MED-Q	Tw_{max}/MVC
1	Male	50	180	90	55.76	16.47	15.96	12.29	10.96	29.54%
2	Male	40	181	81	57.60	11.44	10.97	10.85	10.1	19.86%
3	Female	45	161	50	30.93	7.71	7.25	7.76	6.72	24.93%
4	Female	27	159	54	20.47	6.11	5.94	5.91	5.23	29.85%
5	Male	26	183	74.8	49.27	17.35	16.89	15.9	14.19	35.21%
6	Female	26	168	65.3	32.80	8.60	7.92	6.78	4.37	26.22%
Mean	3:3	26-50	172	69.2	41.14	11.28	10.82	9.915	8.592	27.6%
SD			10.7	15.6	15.17	4.7	4.65	3.82	3.79	5.21%
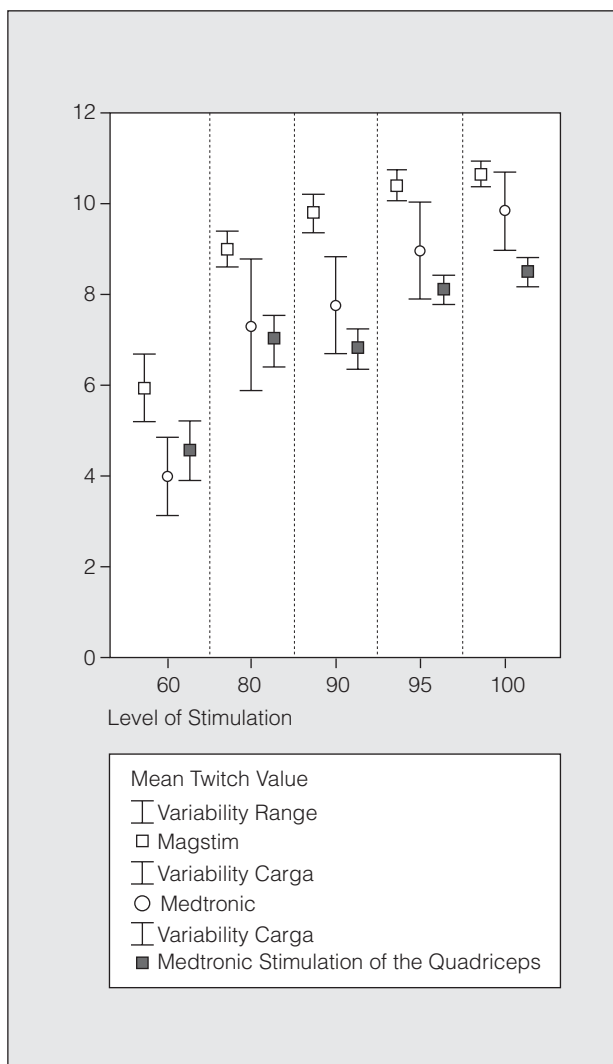
Figure 3. Mean response to different levels of twitch stimulation with the reference Magstim device, the Medtronic device, and the Medtronic device with direct stimulation of the quadriceps. The bars represent intraday coefficients of variability. Note that the double coil of the Magstim device applied to the femoral region and the circular coil applied to the muscle mass (Medtronic device with quadriceps stimulation) reached a plateau, whereas inguinal stimulation with the circular coil of the Medtronic device did not.

Statistical Analysis

Readings from the different maneuvers were recorded and the maximum absolute twitch values and the mean values at each level of stimulation were calculated for each subject and for each of the operations described. Differences in twitch values were calculated between the different application sites and tested statistically using the Student *t* test. A *P* value of less than .05 was considered statistically significant.

The coefficient of variability (CV) for the technique on 2 different days was defined as the mean of the differences in the absolute value divided by the average of the readings and multiplied by 100 (to express the CV as a percentage).

Given that MAG was considered the reference technique, the paired data from the MAG readings were compared with the MED and MED-Q readings to determine the correlation values.

Results

Measurements

All subjects tolerated the procedure well and had no trouble completing the study. The Table shows the data for maximal voluntary contraction, twitch stimulation, and the ratio of the 2 expressed as a percentage, along with anthropometric data.

A comparison of the performance of the 2 systems with different degrees of stimulation is shown in Figure 3. We emphasize that the highest values for twitch stimulation were obtained with the reference MAG equipment, with a mean value for twitches at 100% stimulation of 10.74 kg compared to 9.86 kg for MED and 8.54 kg for MED-Q.

When the tests were repeated on different days, minimal differences were observed between the first and second days. Thus the mean (SE) difference was –0.1849 (0.22) for MAG and –0.0253 (0.333) for MED; these differences were not significant (*P*=.44 and .94, respectively).

The dispersion of the measurements was, however, greater with MED compared to MAG. At maximum stimulus (100%), the interday CV was 17.99% for MED compared to 5.06% for MAG and 6.84% for MED-Q. The intraday CVs were 1.52%, 1.47%, and 1.94% for MED, MAG, and MED-Q, respectively. As shown in Figure 3, the variability in MED measurements was even greater for all submaximal levels of stimulation. We also found that MED-Q yielded a response equivalent to 81% of MAG but without the variability associated with stimulation of the inguinal area using the MED device.

As reflected by the data presented in Figure 3, a supramaximal stimulus—as indicated by a plateau in the response with increasing stimuli—could be discerned for MAG and MED-Q stimulation but not for MED stimulation.

Figure 4 shows the paired data obtained with both stimulation devices. On overlaying plots for both the mean data at 100% stimulation (Figure 4, left panel) and maximum values obtained (Figure 4, right panel), twitch values with MED stimulation are clearly lower than those with MAG stimulation. The linear regression line was below the line of equivalence, although some points of the plot lay on it. For stimulation of the thigh with the circular coil (MED-Q), the linear regression line diverged even further from equivalence, but the values for the coefficient of determination (*r²*) were similar.

Stimulus–response curves were plotted for the 6 volunteers to assess whether supramaximal stimulation was reached with MAG and MED with femoral application (Figure 2). Supramaximal stimulation was observed with MAG in all cases, whereas a plateau in the response could only be observed in 2 volunteers with the MED stimulator (Figure 2, right panel).

Indications

This technique does not require patient cooperation and so can be applied in any clinical setting provided it is not contraindicated. Incorrect execution of maximal voluntary
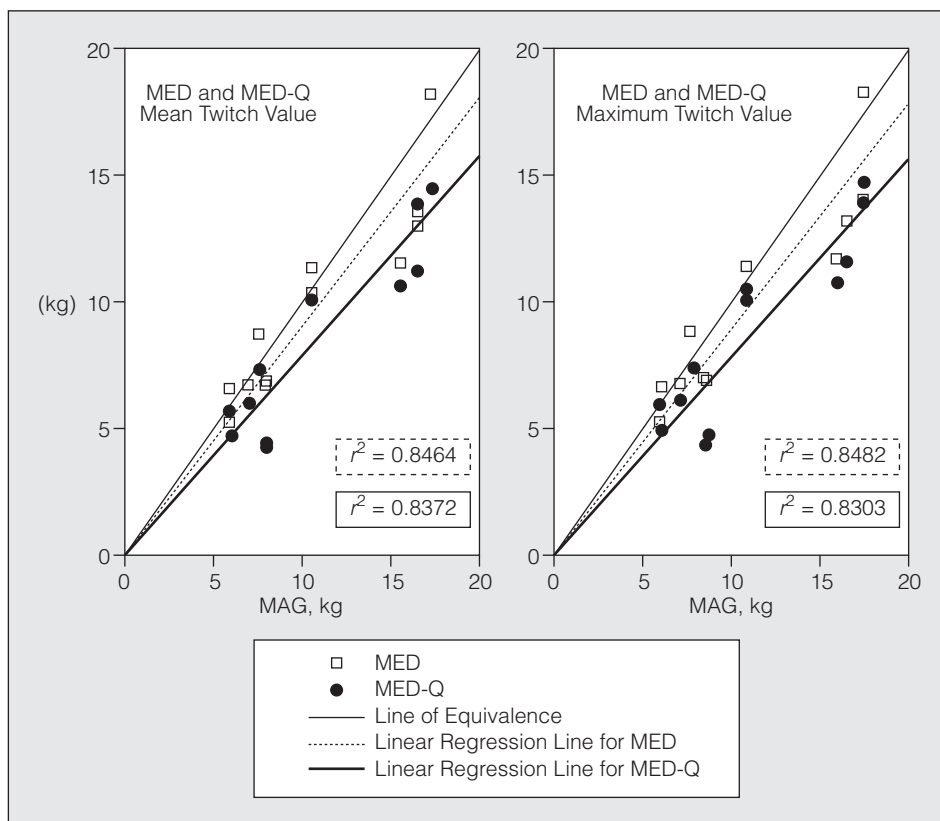
Figure 4. Paired data for the Magstim (MAG) device compared to the Medtronic device (MED) and the MED device with quadriceps stimulation (MED-Q) at 100%. The left panel shows mean values at 100% stimulation. The right panel shows maximum response with twitch stimulation (Tw$_{max}$). The diagonal line, indicating equivalence of the tests, is compared with the linear regression lines for MED and MED-Q. Coefficients of determination (r^2) are shown.

contraction has been reported in a high proportion of patients with COPD, even when they are in a good clinical or neurological state.[17] This, along with the possibility of a learning effect with repetition of the tests, makes it preferable to carry out involuntary maneuvers when assessing muscle response after rehabilitation or other interventions with systemic repercussions.

In respiratory medicine, this technique is of particular interest in the study of patients with stable COPD and in those with exacerbations as a way of assessing the impact of the disease on systemic muscle function.[7] In patients confined to an intensive care unit or bed-bound for long periods of time, monitoring muscle function may be useful for diagnosis and follow-up of emergent neuromuscular disorders. Furthermore, study of the set of inspiratory muscles[23] and peripheral muscles helps in predicting the course of weaning and the physical recovery of these patients and it can indicate whether rehabilitation is necessary. The study of peripheral muscles complements noninvasive study of respiratory muscles, and uses the same diagnostic equipment.

Twitch stimulation of the quadriceps is specifically indicated as part of the examination of patients —particularly children—with neuromuscular diseases. Although the role of pulmonologists is centered on dealing with compromised ventilatory muscle function, cough, or swallowing, involuntary techniques are also needed for studying inspiratory muscles. These techniques can also be applied to studies of such peripheral muscles as the quadriceps.

Contraindications

Since the introduction of magnetic stimulation, there has been speculation about possible adverse effects. However, unexpected or significant effects have not been reported even in cases of repeated transcranial stimulation.[14]

The presence of metal objects where the stimulation field is applied and, above all, proximity to a pacemaker susceptible to damage are clear contraindications for magnetic stimulators.[14] It is normal practice to avoid magnetic stimulation in pregnant women, even though there is no evidence of effects on the fetus. Another effect that has only been reported after repeated stimulation in animals is aural damage, which could be avoided with protective measures.

Discussion

We present data obtained with different devices and coils for magnetic stimulation of the quadriceps. These devices are designed for both diagnostic purposes (twitch stimulation of the quadriceps) and therapeutic ones, that is, muscle training. Our results confirm the suitability of the MAG device with the butterfly coil for obtaining readings with twitch stimulation of the quadriceps. With the MED device coupled to the circular coil, slightly lower values were obtained and supramaximal stimulation was not always reached. When the quadriceps were directy stimulated, a significant response was obtained—equivalent to 80% of the maximum twitch stimulation—and the

response profile indicated that a large portion of the muscle was being supramaximally stimulated.

With the technique described for MAG,[15] twitch stimulation of the quadriceps provided reproducible, supramaximal measurements. For all 6 healthy volunteers, the stimulus was supramaximal according to the plots of the stimulus–response curves (Figure 2, left panel), with a response plateau generally occurring at values between 90% and 100%. The reproducibility, expressed as CV, and the values obtained with twitch stimulation were within the limits reported in the publication of reference on this technique.[15] Values for men were between 11 and 17 kg.

While validating the twitch measurements with the reference device, we also analyzed the performance of the alternative device, MED, a magnetic stimulator that is able to emit trains of impulses at frequencies of up to 30 Hz and that is equipped with a refrigerated coil to prevent overheating during repeated stimulations. This equipment has wider potential uses than MAG, both for neurophysiological diagnosis and in rehabilitation programs. Its diagnostic usefulness for specific measurements with twitch stimulation of the quadriceps had not been previously assessed. Perhaps because of this, when we started our study, no coil equivalent to that used with the MAG device was commercially available so we used a circular 60 mm coil. This equipment did not generate the same values with twitch stimulation as the MAG device, although they were close—92% of the values obtained with twitch stimulation using MAG. This and the fact that we did not reach supramaximal stimulation in some of the volunteers (Figure 2, right panel) can perhaps be attributed to the characteristics of the magnetic field generated by the circular coil. Other authors, also using the MAG device, reported difficulties reaching supramaximal stimulation with circular coils.[14,15] It therefore follows that the double coil which concentrates the magnetic field at the most accessible point of the femoral nerve is a fundamental requirement for achieving supramaximal twitch stimulation. However, even without this type of coil, maximal twitch values were reached in our study with the MED device coupled to a circular coil (Figure 4, right panel), and these values did not differ greatly from those reached with the MAG device. The dispersion and greater variability of the measures may arise because adjusting and positioning the field is more difficult with the circular coil than with the figure-of-eight or butterfly coil.

We decided to assess stimulation of the quadriceps with the circular coil, as repeated stimuli are possible with the refrigerated MED coil. Training protocols based on repeated stimulation would therefore be feasible with such stimulation. Repeated stimulation has the precedent of electrical stimulation of the quadriceps, which has been used by several authors in patients with very severe COPD.[19-21] When such patients have missed the window of opportunity for conventional rehabilitation,[22] that is, when peripheral muscle training becomes impossible due to respiratory limitations, a basic technique in any rehabilitation program—isolated stimulation of muscle groups with lower oxygen consumption—can be considered as a valid option.[18] The results obtained with electrical

stimulation have demonstrated significant improvements in the strength of the leg musculature,[19,20] distance covered in the 6-minute walk test,[20,21] maximum exercise tolerance and resistance,[19] and dyspnea.[19] The improvements in muscle function and exercise capacity have correlated well with the reduction in perception of leg effort corrected for exercise intensity.[19]

In electrical stimulation, the stimuli are applied by surface electrodes over the muscle. With this technique, the response can be varied by activating a larger or smaller portion of the muscle, depending on the strength of the electrical stimulus, which is essentially limited by the pain produced.[24] Han et al[18] determined a tolerance threshold for electrical stimuli whereby only 40% of the maximum contraction could be reached in subjects with intact sensory function. In contrast, magnetic stimulation has the advantage of being painless and having a wider range of tolerance, thus allowing stronger contractions for more effective training regimens, and the results have been promising.[23]

In our study, we aimed to investigate what happens when a magnetic stimulus is applied directly to the muscle. Activation of the branches of the femoral nerve within the muscle would not be considered a nerve twitch stimulation, in which all motor units are activated. A large proportion of these units are however stimulated in their intramuscular branches, with the advantage from the anatomical point of view that the superior and anteroexternal area of the muscle is easier to locate than the inguinal triangle. The sensory innervation in this area of the muscle is also less extensive, so the patient experiences less discomfort. Even though the entire muscle was not stimulated, our volunteers achieved isometric contractions equivalent to 80% of the maximum twitch stimulation (Figure 4). This level is high enough for magnetic stimulation to be used in muscle training[23] for rehabilitation. The level achieved and the fact that this stimulation approached a plateau suggest that almost the entire muscle covered by the magnetic field was stimulated. These data are in agreement with those reported by other authors such as Kremenic et al,[24] who obtained a similar percentage strength (72%) with repeated high-frequency stimulation. These authors determined that the threshold needed to induce muscle gain in the stimulated muscle was 60% of the maximum voluntary contraction.

In conclusion, this study confirmed that magnetic stimulation can be useful for evaluating quadriceps strength. Such an involuntary maneuver is associated with lower variability. Likewise, our study confirmed the need to use coils that are suited to the anatomical site of stimulation (butterfly coils in the inguinal region). Finally, this study showed that magnetic stimulation with direct application to the muscle can induce sufficient contraction to be useful in training protocols. This provides a rationale for using this type of stimulation in rehabilitation strategies for patients with COPD.

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