Muscle Fatigue Evaluation in the Follow-Up of Children Affected by Duchenne Muscular Dystrophy

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Abstract

The aim of this study is to present an original protocol to objectively evaluate the electrical manifestations of muscle fatigue in dystrophic patients and to demonstrate its suitability to clinical applications.

First, we compared electrical manifestations of muscle fatigue in a group of children affected by Duchenne muscular dystrophy and in a control group. We demonstrated that the initial value of muscle fiber conduction velocity is significantly lower in patients than in controls. We also demonstrated that, during standardized electrically elicited contractions, the percent decrement of the power spectrum mean frequency of the surface myoelectric signal is significantly lower in patients with respect to controls.

Then, we applied the evaluation protocol to two groups of patients that underwent a pharmacological trial lasting 24 months. During the first 12 months, one group was given deflazacort 1 mg/kg/day, while the other group was on placebo. Muscle function deteriorated more remarkably in untreated patients, as shown by surface electromyography and by functional evaluation.

During the second 12-month period all the patients were treated. We demonstrated that both groups showed a slow progression of the disease, although patients treated since the beginning of the trial maintained a definitely higher functional index.

It is concluded that the study of the electrical manifestations of muscle fatigue is a valuable tool for non-invasively assessing muscle function in Duchenne patients and for demonstrating the effects of pharmacological treatments.

Key words: surface myoelectric signal, muscle fatigue, electrical stimulation, Duchenne Muscular Dystrophy.

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Duchenne Muscular Dystrophy (DMD) is a lethal disorder of the childhood, transmitted by X-linked recessive inheritance. Nearly all the patients are boys. The disease is present at birth, becomes symptomatic during the early childhood, and leads to the patient death before the end of the third decade of his life. During the progression of the disease there is a progressive decrement of muscle strength mostly due to the necrosis of muscle fibers that are replaced by connective tissue [14]. Several authors demonstrated that the oral administration of corticosteroids attenuates the progression of the disease [1, 7, 11, 15, 17], generally with tolerable side effects.

Muscle fatigue is the result of different events that take place in the central nervous system, in the peripheral nervous system, and in the muscle tissue. Fitts, in his recent review [16], asserts that the main contribution to muscle fatigue is due to events that take place within the muscle fibers.

Even though the definition of muscle fatigue is not unique, there is no doubt that fatigue is a phenomenon that starts at the very beginning of the muscle contraction and becomes evident when the subject is no longer able to maintain a preset level of force [2, 10, 3].

The study of the electrical manifestations of muscle fatigue originates from the observation that, during a sustained contraction, there are visible changes of the surface myoelectric signal due to a progressive compression of its power spectrum towards the lower frequencies [24] and a characteristic bell-shaped variation of its power [9].

The fundamental aspects of the electrical manifestations of muscle fatigue are reported in [3, 10, 2]. It is important to notice that the electrical manifestations of muscle fatigue during a sustained contraction are correlated with the production of catabolites in the muscle tissue and with their removal rate. Thus, patients affected by pathologies that cause a reduction of the muscle fiber density, such as DMD [14, 12], are expected to show reduced electrical manifestations of muscle fatigue. Moreover, the amount of reduction with respect to healthy controls is supposed to be an index of the progression of the pathology.

The electrical manifestations of muscle fatigue are usually investigated by analysing surface myoelectric signals detected during isometric voluntary or electrically elicited contractions [21]. This analysis allows to obtain the time course of different amplitude and spectral parameters during the sustained contraction. Also the time course of muscle fiber conduction velocity is computed from surface myoelectric signals, as explained elsewhere [19].

The most relevant aspects of the electrical manifestations of muscle fatigue are summarized by a diagram referred to as muscle fatigue plot, that presents the time course of a) the mean frequency of the power spectrum of the signal (MNF), b) the root mean square value (RMS), and c) muscle fiber conduction velocity (CV). In the fatigue plot each variable is normalized with respect to its initial value. Some examples of fatigue plots are reported by figure 2 and figure 4.

The observations reported above support the hypothesis that the electrical manifestations of muscle fatigue are a convenient method for assessing the progression of degenerative muscle pathologies in longitudinal studies, as well as for objectively evaluating a specific condition of muscle function in normal and in pathological subjects.

This paper describes an evaluation protocol we developed and applied on patients suffering from Duchenne muscular distrophy and describes some preliminary results of our studies. It must be emphasized that this protocol is not proposed as a diagnostic aid, but as a method to objectively quantify some specific aspects of muscle function mainly related to the propagation of depolarization along the muscle fiber membrane.

In particular we demonstrate that I) the electrical manifestations of muscle fatigue are clearly different in DMD and healthy children, II) our protocol, applied to patients undergoing a pharmacological trial, allows to evaluate objectively the effect of deflazacort on muscle function, and III) treated children and controls show a clearly different behavior over 24 months of follow-up.

Materials and Methods

In this paper we present the results of two different studies. First, we applied the evaluation protocol described below to a group of DMD children and to a control group to establish which, among the observed parameters, best discriminates the two populations. Then, after demonstrating that our protocol clearly differentiates healthy and DMD children, we applied it to the follow-up of DMD patients participating a pharmacological trial.

The first part of the study was carried out on two groups of 20 subjects each. One group consisted of 20 DMD children whose age ranged between 60 and 120 months (mean 87); each patient was able to walk with no support and most patients were able to climb stairs and perform the Gowers manoeuvre. Contractile force expressed by ileopsoas, quadriceps, triceps brachii, and deltoid was evaluated according to the MRC scale [27] and ranged between 70% and 100%. All the patients belonging to this group were never treated by corticosteroids prior to this study. The control group consisted of 20 healthy children with similar age distribution (mean 104), body size, and weight.

The second part of the study was carried out on two groups of DMD patients. The first group consisted of 5 children who showed a very similar value of a functional impairment index (GSCG, see Appendix); they were examined, according to the protocol presented below, prior to starting a pharmacological trial during which they were given deflazacort (1 mg/kg/day); the test was repeated approximately every two months during an observation period lasting 24 months. The second group consisted of 4 children with GSCG values similar to those of the first group; they underwent the same evaluations carried out on the first group, but during the first 12 months of the study they were on placebo. During the second year of the study they were treated as the first group.

Evaluation protocol

Each subject lay supine on an examination table with his dominant foot bound in an isometric brace equipped with a torque transducer. The ankle joint was fixed at 30° of plantar flexion, to allow patients with retraction of the Achilles tendon to comfortably undergo the examination.

Muscle fatigue evaluation was performed on the Tibialis Anterior muscle, because of the relatively extensive body of data available on its structure and behavior and of its suitability for CV measurements [19, 21].

During a preliminary phase, the subject was instructed to attempt plantar dorsiflexion mainly activating the Tibialis Anterior muscle, then he was asked to exert the maximum contraction force (MVC) for approximately 3 s. After a resting period lasting 60 s the contraction was repeated with the same modality. A total number of three contractions was performed, and the highest of the three values of torque was taken as the 100% MVC.

The detection probe was then positioned on the skin, previously cleaned with alcohol, between the most distal motor point and the tendon, as suggested by Roy et al. [26]. The position of the detection probe was then slightly modified in order to find the place in which, during short (3 s) voluntary contractions at 80% MVC, the estimated muscle conduction velocity was the lowest and other specific criteria [26] were met.

After instructing the subject to match and maintain a force target shown on the analog scale of the force trans-

ducer, he was asked to perform an 80% MVC contraction lasting 30 s. Myoelectric signals and torque were sampled and recorded as explained below.

The subject was then prepared for the electrically elicited contractions. The motor points of the Tibialis Anterior muscle were identified as those with the lowest stimulation threshold, and their position marked on the leg.

To electrically stimulate the muscle, a circular (25 mm diameter) negative sponge-electrode was placed on its most distal motor point. A large rectangular (12 cm x 8 cm) positive sponge-electrode was placed on the gastrocnemius muscle. The current lines would thus traverse a roughly conical space across the leg along the tibia bone.

First, the position of the circular stimulation electrode was slightly modified, until the muscle could exert the highest force during short (5 s) electrically elicited contractions. The frequency of stimuli was fixed to 35 Hz because it allows for fast fatiguing the muscle while M-waves are still clearly separated [21]. Supramaximal stimulation was obtained by increasing the stimulus intensity until the M-wave reached its maximum peak to peak value, and then setting the stimulation level approximately 10% above that generating the maximal M-wave.

The position of the detection probe was then adjusted to meet the same criteria cited above. After a resting period lasting 5 min the subject performed an electrically elicited contraction lasting 30 s. Stimulation parameters were set as above. Again, myoelectric signals and torque were sampled and recorded.

Signal detection and processing

The myoelectric signal was detected with the four-bar active electrode described by Broman et al. [6]. Interelectrode distance was equal to 10 mm. A single differential signal was obtained from the two central bars and was used to compute MNF and RMS.

Muscle fiber conduction velocity was estimated by aligning in the frequency domain the Fourier transforms of two adjacent double differential signals. This procedure is reported elsewhere [19].

Avoiding or removing the stimulation artifact is a common problem when electrically elicited potentials must be analyzed. We solved this problem by using a specific stimulation and detection system previously developed, that usually allows to keep the stimulation artifact below the noise level [18].

Myoelectric signals and the torque signal were amplified, bandpass filtered (10 Hz - 470 Hz), sampled by means of a 12 bit A/D card with a sampling frequency equal to 1024 Hz, and stored on the hard disk of a 486 MS-DOS personal computer.

During the acquisition, the signal quality was checked by on-line displaying the signals on the monitor of the personal computer.

Signals detected during each contraction were segmented in 1 s epochs. MNF, RMS, and CV were then computed over each epoch, tabulated, and their time course plotted. Details of signal processing are reported elsewhere [22].

Several indexes have been proposed in literature to quantify the electrical manifestations of muscle fatigue. In the following we adopt a specific index, referred to as *overall MNF percent decrement* ($\Delta\%_{MNF}$).

$$\Delta\%_{MNF} = \frac{MNF_i - MNF_j}{MNF_i} * 100$$

where:
MNF_i = value of MNF computed during the first 1-second epoch (at the beginning of the contraction);
MNF_f = value of MNF computed during the last 1-second epoch (at the end of the contraction).

The evaluation protocol is completely non-invasive and discomfort due to electrical stimulation is minimal. The time required to carry out the entire evaluation session is approximately 35-40 min. This evaluation was always well accepted by DMD children and controls.

Results and Discussion

Differences between DMD patients and controls investigated by means of surface electromyography

In order to assess the differences between DMD children and controls, we studied two groups of 20 children with similar age distribution by applying the evaluation protocol described above.

MUSCLE FIBER CONDUCTION VELOCITY

Figure 1 shows the histogram of the muscle fiber conduction velocity estimated in the control and DMD groups during the first second of an 80% MVC voluntary contraction. Since the values were estimated at the very beginning of the contraction, they were not affected by fatigue. In normal subjects CV ranged from 3.5 m/s to 5.5 m/s, while in DMD children it was comprised between 2 m/s and 3.5 m/s.

Statistically, values relative to the DMD group are lower than those obtained from the control group (two-sample t-test, $p \leq 0.001$). We obtained similar results by comparing initial CV values obtained during electrically elicited contractions.

Our observation is in agreement with results reported by Ramaekers et al. [25], who examined 17 DMD children aged between 60 and 120 months. It is worthy to observe that the cited work was carried out by using a different methodology for estimating CV.

From a physiological point of view, it is well known that CV is related to nonlinear channel conductivities [23], intracellular and extracellular pH level [23], and muscle fiber crossection [23].

The reduced average CV value in DMD children with respect to controls may be ex-plained by the following observations: a) in DMD children it was observed an increment of the proportion of type I fibers [12, 13], that in the Tibialis Anterior generally have a smaller crossection than type II muscle fibers [19] and consequently also a reduced CV value; b) regenerating fibers are a constant finding in DMD, and it takes an indetermined amount of time for them to mature and reach a normal girth size [14];

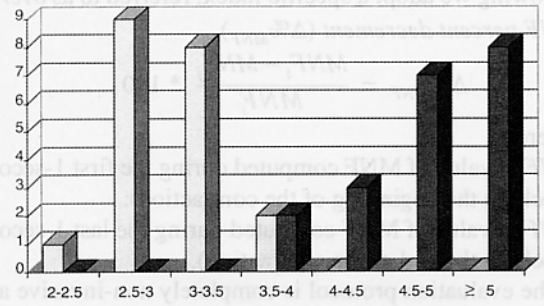

Figure 1. Histograms of the initial value of muscle fiber conduction velocity in children suffering from Duchenne muscular dystrophy (light grey, n = 20) and controls (dark grey, n = 20). These values were estimated at the very beginning of a voluntary contraction at 80% MVC. The initial value of muscle fiber conduction velocity is statistically lower in patients than in controls (Two sample t-test, p ≤

it is likely that regenerating fibers show a low CV value until their final size is reached, and thus they could contribute to a reduction of the average CV value; c) several Authors [5, 8, 28] demonstrated plasma membrane defects in nonnecrotic fibers of DMD patients; these structural abnormalities could affect the time course of the depolarization and ripolarization of the muscle membrane, and then be responsible for decreased CV.

At this time it is not possible to determine to which extent the three phenomena cited above contribute to the reduction of CV observed in DMD patients. Further studies are needed to clarify this issue.

ELECTRICAL MANIFESTATIONS OF MUSCLE FATIGUE: VOLUNTARY CONTRACTIONS

Figure 2 presents the fatigue plots obtained respectively from a DMD patient (a) and a control subject (b) during an attempted constant force and isometric voluntary contraction. By reason of the large variability of the time course of the observed variables, the fatigue plots relative to voluntary contractions do not allow to clearly differentiate patients from controls.

The scarce capability of differentiating the two groups is due to the fact that voluntary contractions suffer from several drawbacks, that limit their clinical applicability: a) if subjects are not willing or able to fully cooperate, it is difficult to ascertain that the 100% MVC value actually corresponds to their maximum contraction force; this difficulty is particularly considerable with DMD children; b) during sustained voluntary contractions, the values of spectral and amplitude parameters are affected by the stability of the motor unit pool as well as by the firing rate of each specific motor unit; it must be emphasized that the motor unit pool and individual firing rates may change even if the output force is kept constant.

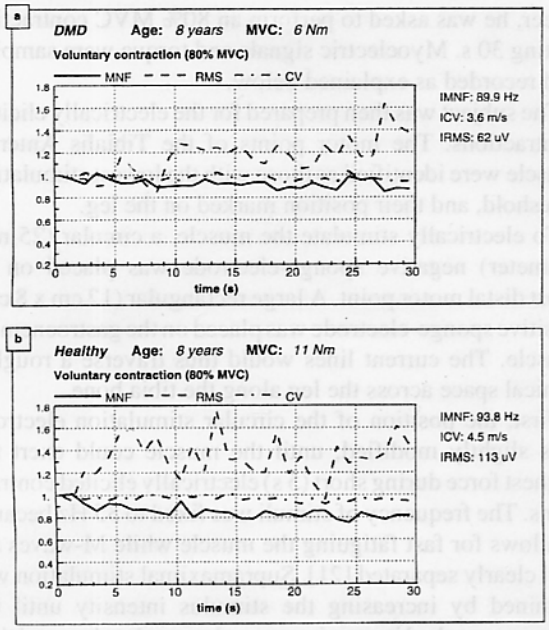

Figure 2. Time course of MNF (solid line), RMS (dashed line), and CV (dash-dot line) during an isometric voluntary contraction at 80% MVC. The upper frame (a) shows the fatigue plot of an 8 years old DMD child; the lower frame (b) presents the fatigue plot of a control. The three variables are normalized with respect to their initial values.

The observations reported above demonstrate that voluntary contractions are not a suitable exercise modality to study the electrical manifestations of muscle fatigue in DMD children.

ELECTRICAL MANIFESTATIONS OF MUSCLE FATIGUE: ELECTRICALLY ELICITED CONTRACTIONS

Figure 3(b) presents the fatigue plot obtained from a control subject during an electrically elicited contraction. It is important to underline that fatigue plots obtained from controls are generally very similar, and the $\Delta\%_{MNF}$ ranges from 40% to 45% of its initial value and is independent from the patient age.

Figure 3(a) presents the fatigue plot obtained from a 9 years old DMD child. It is evident that the three variables show a reduced variation during the contraction. Particularly MNF, that is the most sensitive to localized muscle fatigue [21], shows a $\Delta\%_{MNF}$ slightly smaller than 15%.

The reduced $\Delta\%_{MNF}$ in patients with respect to controls is evident even when the two groups are compared. Figure 4 shows the histogram of $\Delta\%_{MNF}$ in DMD patients and controls. While controls show a $\Delta\%_{MNF}$ comprised between 40% and 50%, all the DMD children present a $\Delta\%_{MNF}$ lower than 30%.

Again, values relative to the DMD group are statistically lower than those obtained from the control group (two-sample t-test, $p \leq 0.001$). Moreover, although the number of patients is too small for obtaining an acceptable con-

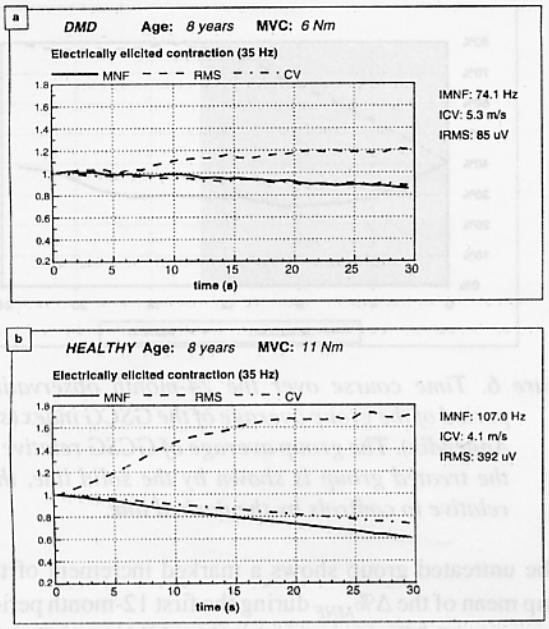

Figure 3. Time course of MNF (solid line), RMS (dashed line), and CV (dash-dot line) during a supramaximal electrically elicited contraction. Stimulation frequency was equal to 35 Hz. The upper frame (a) shows the fatigue plot of an 8 years old DMD child; the lower frame (b) presents the fatigue plot of a control. The three variables are normalized with respect to their initial values. It is evident the smaller variation of the observed parameters in frame (b).

fidence level, our data support the hypothesis that the $\Delta\%_{MNF}$ obtained during electrically elicited contractions decreases with the progression of the disease. If supported by further investigation, this observation could be important for obtaining an objective clinical score of muscle impairment in these patients.

The reduction of the $\Delta\%_{MNF}$ relative to an electrically elicited contraction observed in DMD children may be explained by the following considerations.

It was demonstrated that the percent decrement of CV ($\Delta\%_{CV}$) and $\Delta\%_{MNF}$ are proportional to the amount of catabolites produced by muscle fibers during their activity. This statement is supported by a previous work [21], in which it was demonstrated that by increasing the stimulation frequency in steps equal to 5 Hz the $\Delta\%_{CV}$ and $\Delta\%_{MNF}$ increased monotonically.

Moreover, Brody et al. [4] demonstrated that hamster diaphragm fibers kept in an oxygenated and buffered bath showed a strong correlation between the bath pH and their MNF and CV. Since during a contraction the pH values of the interstitial and intracellular fluids are known to significantly decrease [16], it follows that CV and MNF decrements observed during muscle contraction are related to H^+ ion production.

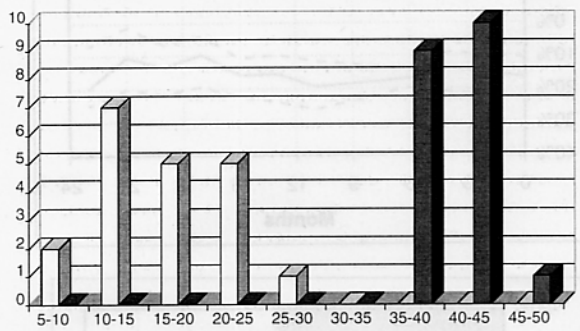

Figure 4. Histograms of the percent decrement of MNF during an electrically elicited contraction lasting 30 s in children suffering from Duchenne muscular dystrophy (light grey, n = 20) and controls (dark grey, n = 20). Stimulation frequency was equal to 35 Hz and the stimulus intensity was supramaximal. The MNF percent decrement is statistically lower in patients than in controls (Two sample t-test, $p \leq 0.001$).

If the stimulation frequency is fixed, the amount of catabolites produced by a contracting muscle in the unit of time is proportional to the average number of muscle fibers per square unit of the muscle crossection. It is well known that DMD patients undergo a progressive replacement of contractile by connective tissue elements [14]. Then, with the progression of the disease, the average number of muscle fibers per square unit of muscle crossection decreases, thus decreasing the amount of catabolites (and H^+ ions) produced during a standardized contraction.

It follows that the reduction of the $\Delta\%_{MNF}$ observed in DMD children should be roughly proportional to the area of connective tissue per square unit of muscle crossection, and then this parameter could give an objective measure of the progression of the disease.

Electrical manifestations of muscle fatigue in longitudinal studies: preliminary results

The main reason for developing objective evaluation procedures of the muscle function is to provide physicians with a reliable evaluation methodology to document the effect of different treatments aimed at lessening the progression of the disease.

Here we present preliminary results obtained by evaluating $\Delta\%_{MNF}$ during a 35 Hz supramaximal stimulated contraction of the Tibialis Anterior, lasting 30 s, in two groups of DMD children, over an observation period lasting 24 months.

Figure 5 presents the mean value (solid line) of the $\Delta\%_{MNF}$ obtained within each evaluation session during the 24-months period. The two dotted lines depict the extreme values of the observed variable, recorded during each

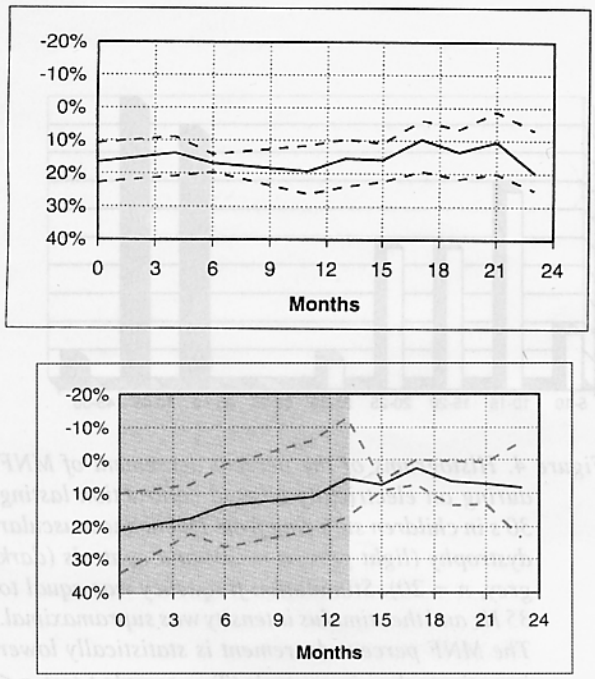

Figure 5. Time course over the 24-month observation period of the group average of the percent decrement of MNF relative to supramaximal electrically elicited contractions at the stimulation frequency of 35 Hz. The upper frame shows the group average (solid line) and the region that contains the values relative to all the five subjects (bounded by dashed lines). The lower frame is relative to four patients on placebo during the first 12 months (shaded region) and then treated as those belonging to the first group.

evaluation session, in the group. Data relative to the treated group are reported in Figure 5(a) while those relative to the placebo group are presented in the shaded region of Figure 5(b). The unshaded region of this figure is relative to the same group during the second 12-month period, in which also these patients were treated according to the protocol briefly presented above.

The analysis of the two figures demonstrates that the treated group shows a constant value of the group mean $\Delta\%_{MNF}$ over the first 12 months (run test, $p \leq 0.05$), while the same variable shows a positive trend from month 12 to the end of the observation period (run test, $p \leq 0.05$).

It is worthy to emphasize that a decreasing behavior of this variable is associated with decreased electrical manifestations of muscle fatigue and hence, in our opinion, with an increment of the proportion of connective tissue in the muscle crossection. It follows that during the first 12 months the treated children show, in average, a stable behavior of the observed variable, thus demonstrating some positive effects of the treatment on muscle function. From the 12th month to the end of the treatment there is a slight progression of the pathology.

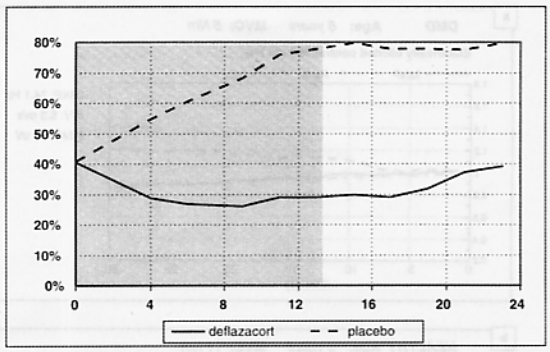

Figure 6. Time course over the 24-month observation period of the group average of the GSCG index (see Appendix). The group average of GCSG relative to the treated group is shown by the solid line, that relative to controls by the dashed line.

The untreated group shows a marked increment of the group mean of the $\Delta\%_{MNF}$ during the first 12-month period (run test, $p \leq 0.05$), demonstrating that children on placebo show a constant progression of muscle impairment. This tends to stabilize when the treatment starts (12^{th} month).

Figure 6 shows the GSCG average score of the two groups over the 24-month observation period. Treated children (solid line) show an initial improvement of muscle function that tends to stabilize after approximately one year. Starting from the 18th month, their GSCG score shows an increment and reaches approximately its value prior to the treatment, thus demonstrating that muscle function declines again after an improvement lasting approximately 16-18 months.

This behavior is consistent with that showed by $\Delta\%_{MNF}$ on the same group, but it seems that the latter is able to detect the beginning of the worsening trend approximately 4 months in advance with respect to GSCG.

Untreated children show a marked increment of their average GSCG score, that stops when the treatment starts. Again, this behavior is consistent with that of $\Delta\%_{MNF}$ shown in Figure 5(b).

First it is important to observe that electrical manifestations of muscle fatigue represented by the $\Delta\%_{MNF}$ and the functional impairment index (GSCG) show consistent variations for both groups during the 24 months of observation. It is suggested that electrical manifestations of muscle fatigue obtained during a single electrically elicited contraction are an objective and reliable procedure to assess the effects of coricosteroids administered during pharmacological trials. The time required to carry out this reduced protocol on DMD children is approximately 15 minutes.

Moreover, results herein presented suggest that the behavior of $\Delta\%_{MNF}$ can anticipate significant progressions of the pathology more efficiently than the functional index we adopted. The clinical interest of this observation is remarkable, since it could allow for a well-timed adaptation of the posology to variations of the patient status. It must be

emphasized that, due to the small size of the two groups involved in this study, this interesting characteristic of our methodology has not been demonstrated statistically.

Conclusions

In this paper we present two different applications of a novel evaluation protocol for muscular dystrophies based on the study of electrical manifestations of muscle fatigue during voluntary and electrically elicited muscle contractions.

First, we applied our protocol to a group consisting of 20 DMD children, whose age ranged between 60 and 120 months, and to a control group of 20 subjects, with similar age distribution.

Data herein reported demonstrate that the non-fatigued value of CV is statistically lower in DMD children with respect to controls, thus demonstrating that sarcolemma abnormalities typical of DMD cause modifications of the depolarization process that our methodology is able to detect and quantify.

Moreover, we also demonstrate that electrical manifestations of muscle fatigue are reduced in DMD children with respect to the control group. This finding is tentatively explained by the replacement of muscle fibers by connective and fatty tissue that is typical of the progression of the disease. It is then suggested that our methodology could be used to objectively assess the level of muscle tissue deterioration in different subjects to enforce prognosis, or, during longitudinal studies, to document the effect of pharmacological or rehabilitation treatments.

The second part of this study is relative to the follow-up of 5 DMD patients treated by deflazacort and 4 DMD patients on placebo during the first 12 months of the study and then treated as the first group until the end of the study herein presented, after 24 months.

Data obtained by studying the electrical manifestations of muscle fatigue on these patients demonstrate that treated patients show an appreciable improvement of their muscle function during the first 12 months, that is strongly reduced or stops during the second half of the trial. Patients on placebo show a clear deterioration of their muscle function during the first 12 months, that is strongly reduced, and sometimes partially recovered, when the treatment starts.

Data obtained by evaluating the electrical manifestations of muscle fatigue are consistent with those obtained by applying a specific functional index of muscle impairment (GSCG).

It is concluded that the study of the electrical manifestations of muscle fatigue is a valuable tool for non-invasively assessing muscle function in DMD patients and to document the effects of pharmacological treatments.

Moreover, since the protocol we developed does not depend on the cooperation of the patient, it can be used also to evaluate mentally impaired and/or very young children. It must be emphasized that, by using functional indexes, these patients often show reduced scores primarily due to their difficulty in understanding how to correctly perform the exercise or because of their poor ability to actively cooperate.

Table 1. The evaluation scale of the four tests.

Score	Test			
	Gait (x_1)	Stairs (x_2)	Chair (x_3)	Gowers (x_4)
1	Normal	Normal	Normal	Normal
2	Slightly waddling or lordotic or equinus	One hand on the thigh	With difficulty but no support	Pelvis up first and one hand on floor
3	Mildly waddling or lordotic or equinus	Both hands on the thigh	One hand on the thigh or on the chair	Pelvis up first and both hands on floor
4	Severely waddling or lordotic or equinus	One hand on the rail	Both hands on the thigh or on the chair	One hand on the thigh
5	Only with hortheses	Both hands on the rail	With the help of a table or other chairs	Both hands on the thigh
6	Only keeps upright position ($t = 0$)	Only climbs a few steps	Unable ($t = 0$)	With the help of chairs or other objects
7	Wheelchair ($t = 0$)	Unable ($t = 0$)		Unable ($t = 0$)

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Appendix

GSCG is a functional index that measures muscle impairment. It is obtained by evaluating patient performances in Gait, Stairs climbing, standing up from a Chair, and Gowers manoeuvre.

The GSCG index ranges from 0% to 100%; the lowest value means that muscle function is normal, while the highest is reached when the subject is no longer able to perform any of the four tests that constitute the index.

The value of GSCG is obtained by applying the following formula:

$$GSCG = \frac{\sum_{i=1}^{4} (x_i + t_i/t_{imax}) - 4}{23} \cdot 100$$

where:

x_i = score obtained in each of the four tests (see table 1);

t_i = time needed to complete each of the four tests;

t_{imax} = maximum time allowed to complete each of the four tests (t_1 = 40 s, t_2 = 50 s, t_3 = 30 s, t_4 = 50 s). If a patient fails to complete a test within the maximum time, t_i is assumed as equal to t_{imax}.

- The test of gait consists of evaluating the patient's gait over a distance equal to 10 m.
- The test of stairs climbing consists of evaluating the patient on four step stairs.
- The test of standing up from a chair is performed by utilizing a chair whose size depends on children height.
- Gowers manoeuvre is well known to the clinical community.

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References

[1] Angelini C, Pegoraro E, Turella E: Deflazacort in Duchene dystrophy: study of long term effect. *Muscle & Nerve* 1994; 17 (4): 386-391.

[2] Basmajian JV, De Luca CJ: *Muscles Alive.* Baltimore (MD), Williams & Wilkins, 1985.

[3] Bigland-Ritchie B: EMG and fatigue of human voluntary and stimulated contractions, in: *Human muscle fatigue: physiological mechanisms.* London, Pitman Medical, 1982.

[4] Brody L, Pollock M, Roy SH, De Luca CJ, Celli B: pH induced effects on median frequency and conduction velocity of the myoelectric signal. *J of Appl Physiol* 1991; 71 (5): 1878-1885.

[5] Bradley WG, Fulthorpe JJ: Studies of sarcolemmal integrity in myopathic muscle. *Neurology* 1978; 28: 670.

[6] Broman H, Bilotto G, De Luca CJ: A note on the non-invasive estimation of muscle fiber conduction velocity. *IEEE Trans on BME* 1985; 32: 341-344.

[7] Brooke MH, Fenichel GM, Griggs RC: Clinical investigation of Duchenne muscular Dystrophy. Interesting results in a trial of prednisone. *Arch Neurol* 1987; 44: 812-817.

[8] Carpenter S, Karpati G: Duchenne muscular dystrophy: Plasma membrane loss initiates muscle cell necrosis unless it is repaired. *Brain* 1979; 102: 147.

[9] Cobb S, Forbes A: Electromyographic studies of muscle fatigue in man. *Am J Physiol* 1923; 65: 234-251.

[10] De Luca CJ: Myoelectric manifestations of localized muscle fatigue in humans. *Crit Rev in Biom Eng* 1984; 11: 251-279.

[11] Desilva S, Drachman DB, Mellits D, Kunel RW: Prednisone therapy in Duchenne muscular dystrophy. Long term benefit. *Arch Neurol* 1987; 44: 818-828.

[12] Dubowitz V: *Muscle Biopsy. A practical approach,* England: Baillière Tindall, 1985.

[13] Dubowitz V, Brooke MH: *Muscle Biopsy: A Modern Approach.* London, Saunders, 1973.

[14] Engel AG, Banker BQ: *Myology. Basic and clinical.* New York, McGraw-Hill, 1986.

[15] Fenichel GM, Pestronk FA, Miller JP: Prednisone slows strength decline in Duchenne muscular dystrophy: two years observation. *Neurology* 1991; 41 (suppl. 1), 166: 1825.

[16] Fitts RH: Cellular mechanisms of muscle fatigue. *Physiol Rev* 1994; 74: 49-94.

[17] Griggs RC, Moxley RT, Mendell JR: Prednisone in Duchenne Dystrophy. A randomized controlled trial defining time course and dose response. *Arch Neurol* 1991; 48: 383-388.

[18] Knaflitz M, Merletti R: Suppression of stimulation artifacts from myoelectric evoked potential recordings. *IEEE Trans. on BME* 1988; 35: 758-763.

[19] Knaflitz M, Merletti R, De Luca CJ: Inference of motor unit recruitment order in voluntary and electrically elicited contractions. *J Appl Physiol* 1990; 68: 1657-1667.

[20] Kupa EJ, Roy SH, Kandarian SC, De Luca CJ: Effects of muscle fiber type and size on EMG

median frequency and conduction velocity. *J Appl Physiol* 1995; 78 (1): 23-32.

[21] Merletti R, Knaflitz M, De Luca CJ: Myoelectric manifestations of fatigue in Voluntary and electrically elicited contractions. *J Appl Physiol* 1990; 69: 1810-1820.

[22] Merletti R, Knaflitz M, De Luca CJ: Electrically Evoked Myoelectric Signals. *Crit Rev in Biom Eng* 1992; 19: 293-340.

[23] Miller RN, Rinzel J: The dependence of impulse propagation speed on firing frequency, dispersion, for the Hodgkin-Huxley model. *Biophys J* 1981; 34: 227-259.

[24] Piper H: *Electrophysiologie Menschlicher Muskeln* (German Text). Berlin:, Springer Verlag, 1912.

[25] Ramaekers VTh, Disselhorst-Klug C, Schneider J, Silny J, Forst J, Forst R, Kotlarek F, Rau G: Clinical applications of a non invasive multi-electrode array EMG for the recording of single motor unit activity. *Neuropedriatrics* 1993; 24: 134-138.

[26] Roy SH, De Luca CJ, Schneider J: Effects of electrode location on myoelectric conduction velocity and median frequency estimates. *J Appl Physiol* 1986; 61: 1510-1517.

[27] Scott OM, Hyde SA, Goddard C, Dubowitz V: Quantitation of muscle function in children: a prospective study in Duchenne Muscular Dystrophy. *Muscle & Nerve* 1982; 5: 291-301.

[28] Wakayama Y, Bonilla E, Schotland DL: Muscle plasma membrane abnormalities in infants with Duchenne muscular dystrophy. *Neurology* 1983; 33: 1368.