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Non-Invasive Diagnosis of Neuromuscular Disorders by High-Spatial-Resolution-EMG

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1. Introduction

Neuromuscular diseases are defined as pathological changes of the peripheral nerves (neuronal disorders), the neuromuscular junctions or the muscle fibres (muscular disorders). Since they are accompanied by weakness commonly, they have essential impact on the patient's movement performance. Especially in childhood, the consequences are serious and early diagnosis is essential for an adapted and task orientated therapy. The main aim in diagnostics of neuromuscular diagnosis is to distinguish between patients without any morbid changes in the MUs, patients with muscular disorders, and patients with neuronal disorders. Here, diagnostics avail on the fact that changes in the skeletal muscles, which take place during the progress of the disorder, are mostly on the level of single motor units (MUs). The MU is the smallest unit of the muscle, which can be activated independently by the central nervous system [Basmajian 1985]. Muscular disorders, for example, are characterised by a loss of single muscle fibres. This results in the fact that less muscle fibres contribute to an affected MU than to a healthy one. This is in contrast to neuronal disorders in which the motor neuron is destroyed. Consequently, complete MUs are affected. In this case the number of muscle fibres contributing to a MU is unchanged but the number of MUs available for force generation is reduced [Jerusalem 1979, Dubowitz 1991].

In human movement and locomotion the voluntary and active contraction of a muscle is initiated by the electrophysiological excitation of a pool of MUs. Since Electromyography (EMG) detects the electrophysiological signal generated by the muscle during excitation, it is a well established procedure utilised in studies of muscle function [Basmajian 1985]. During the last years surface electromyography (sEMG) has become more and more important. It offers a number of advantages when compared to invasive EMG procedures, like needle- or wire-EMG. For example, it causes no discomfort or risk of infection due to the insertion of the needle or the wire and it does not require the supervision by a physician. Compared to invasive measurements, the repeatability of surface EMG measurements is superior, and long term monitoring is possible, [Jonsson 1968]. In addition, the conventional needle-EMG is not suitable for investigations of the excitation spread. Compared to the needle EMG the wire EMG is less painful and allows the detection of the excitation spread. But after insertion the wire electrode tends to migrate within the muscle tissue even during isometric contraction [Jonsson 1968, Komi 1970]. Consequently, the reproducibility of the EMG signal detected with wire electrodes is limited.

The conventional sEMG has a limited spatial resolution and detects, therefore, a superposition of a large number of MUs. The separation of the activity of single MUs from simultaneously active adjacent ones is hard to achieve with surface electrodes. This task still needs highly specialised acquisition techniques, [Merletti 1989]. Consequently, sEMG is mainly used to obtain 'global' information about the muscle activation, like timing or intensity of the muscle activation. Therefore, for diagnostic purpose of neuromuscular disorders, the conventional sEMG techniques are not suitable, since information about the single MUs is needed to distinguish between patients without any morbid changes in the MUs, patients with muscular disorders, and patients with neuronal disorders. This is why in clinical practice still invasive Needle-EMG techniques are used, which gain the needed information about the single MU activity. The diagnostic selectivity of the commonly used Needle-EMG-procedures has been determined by comparing the Needle-EMG diagnosis and the result of a muscle biopsy [Hausmanova 1971, Black 1974, Buchtal 1982]. The most significant work is that of Buchtal and Kamieniekwa, which establishes a diagnostic selectivity of the Needle-EMG procedure of 77% in muscular disorders and 91% in neuronal disorders. However, in addition to the non-convincing diagnostic selectivity, the Needle-EMG methods are invasive and, consequently, painful for the patient.

2. High-spatial-resolution-EMG

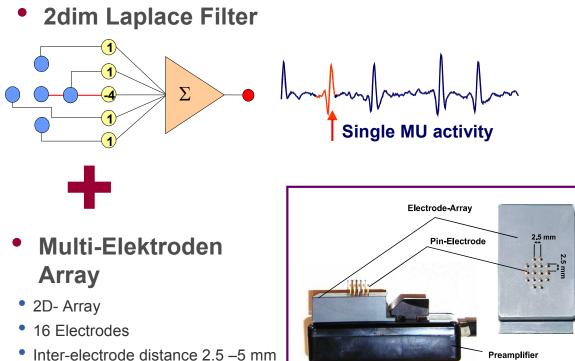
In contrast to the conventional surface EMG techniques, the High-Spatial-Resolution EMG (HSR-EMG) allows the non-invasive detection of the single MU activity even during maximal voluntary contraction of the muscle. The methodology is based on the use of a multi-electrode array in combination with a spatial filter processing [Disselhorst-Klug 1998, Disselhorst-Klug 2000].

During a voluntary excitation of the muscle by the central nervous system, a time variable potential distribution is generated on the skin surface. Multi-electrode arrays can be beneficially used for the detection of the spatial potential distribution generated. From this information about the localisation of the source and its movement in time can be gained. Multi-electrode arrays are commonly used in electroencephalography and are recently becoming more popular in sEMG. In sEMG they have been described first by Rau [Rau1985], Masuda et al. [Masuda1985], De Luca et al. [de Luca 1987] and Reucher et al. [Reucher1987] and have been advantageously used in the fields of neurology, ergonomics, and biomechanics during the last years [Disselhorst-Klug 2000, Rau 2004]. Commonly used multi-electrode arrays consist of several (up to 240) pin-electrodes arranged either in a row or two-dimensionally with an inter-electrode distance of only a few millimetre. A multielectrode array consisting of 16 gold-covered pin-electrodes (Figure 1) for example is used for the diagnostics of neuromuscular disorders. In this case the electrodes have a diameter of 0.5 mm and are springing-fitted to provide optimal contact with the skin surface. They are arranged two-dimensionally and have an inter-electrode distance between 2.5 mm and 5 mm depending on the muscle being investigated [Disselhorst-Klug 2000].

The potentials detected by the different electrodes of the array can be regarded as instantaneous spatial samples of the potential distribution generated on the skin surface by the excitation of the muscle fibres. To this potential distribution contribute different MUs in a different way. A small number of MUs, which are located very close to the skin surface, contribute to the resulting potential distribution with a spatially steep and high potential. On the contrary, MUs which are located more far away from the skin surface contribute

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HSR-EMG



• Electrode diameeter0.5 mm



Fig. 1. HSR-EMG.

Multi-electrode array for the detection of the single motor unit activity during maximum voluntary contractions of the m. abductor pollicis brevis. By using an NDD-filter the single MU activity can be isolated in the signal. Adapted from [Disselhorst-Klug 2000].

lower and spatially more widened potential (Figure 2) [Disselhorst-Klug 1998]. This is due to the fact that caused by the electrical characteristic of the tissue between the source and the skin surface spatially high frequencies in the signal are more suppressed the deeper the source is located in the body [Lynn 1978]. Figure 2 shows an example of the potential distribution generated on the skin surface by two MUs located in different depth. If both MUs are excited at the same time. The potential distribution generated on the skin surface is equal to the superposition of the contributions of both MUs. Conventional sEMG applications are based on a bipolar lead with an inter-electrode distance of about 20 mm [Hermens 2000]. Due to this relatively large inter-electrode distance such an electrode arrangement detects the absolute value of the superimposed potential distribution, to which both MUs contribute in the same manner (Figure 2).

The volume conductor between the excited MU and the skin surface acts like a spatial lowpass filter. On the other hand, a spatial high-pass filter with an adequate cut-off frequency would transmit spatial frequencies higher than its cut-off frequency and would suppress spatially lower ones. Thus, by using a spatial high-pass filter the spatially high frequency contribution of MUs located close to the skin surface will be amplified and the contribution of MUs located more distantly will be reduced.

In a first approach, the simplest spatial high-pass filter - a bipolar lead with an interelectrode distance in the mm-range and arranged in parallel to the muscle fibres - was used to improve the spatial selectivity of the non-invasive EMG-recording techniques (Figure 2) [Lynn 1978]. The bipolar lead differentiates the spatial potential distribution in the direction of the electrode arrangement. Due to this differentiation the bipolar lead enhances spatially steep components and reduces more flat ones (Figure 2). However, particularly at high force levels the bipolar lead with a small inter-electrode distance is not sufficient to discriminate the single MU activity in the signal course. Therefore, the principle of spatial filtering has been extended to more complex electrode arrangements.

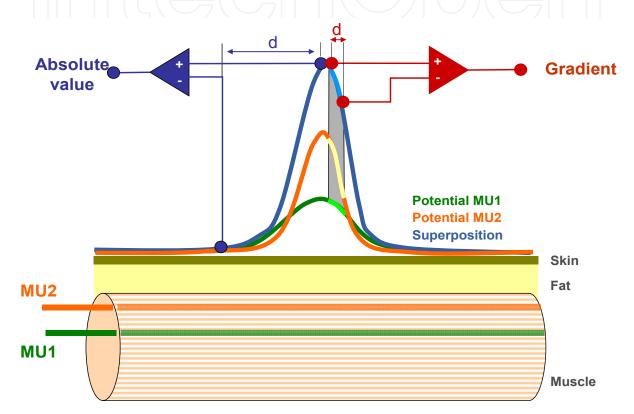


Fig. 2. Potential Distribution.

Potential distribution generated on the skin surface by two MUs located in differed distances from the skin surface. By using electrode distances d in the mm-range the contribution of the MU located close to the skin surface can be emphasised and the contribution of the more distantly located MU can be suppressed. Adapted from [Disselhorst-Klug 2000].

From image-processing it is known, that Laplace filters - which give the second spatial derivative - are well suited for the detection of edges perpendicular to the direction of differentiation. A one-dimensional Laplace filter can be realised with three electrodes arranged in a row. The central electrode has to be weighted with a factor of -2 and the two outer electrodes with a factor of 1. Such double differentiating filters have been first used in sEMG by Broman et al., [Broman 1985], and are now frequently used by different other groups. A higher spatial selectivity of the recording set-up can be achieved with two-dimensional Laplace filter arrangements [Reucher 1987, Disselhorst-Klug 1998]. It has been shown that a weighted summation of five cross-wisely arranged EMG leads forms the

second spatial derivative of the potential distribution in two orthogonal directions (Normal-Double-Differentiating-Filter). To perform a NDD-Filter the central electrode is weighted with a factor of -4 and the surrounding electrodes with a factor of +1. The NDD-Filter amplifies only the activity of MUs located directly below the centre electrode of the filter and reduces the signals of more distantly located sources. In this way, the activity of single MUs becomes clearly distinguishable in the signal course (Figure 1). Thus, the HSR-EMG allows the non-invasive detection of the single MU activity and seems, consequently, to be suitable for a non-invasive diagnosis of neuromuscular disorders [Disselhorst-Klug 1994, Farina 2003].

In initial clinical investigations the HSR-EMG has been validated in children suffering from Duchenne Muscle Dystrophy (Duchenne) or Spinal Muscle Atrophy (SMA) [Ramaekers 1993, Huppertz 1995, Rau 1997, Disselhorst-Klug 2000]. The investigations show that the HSR-EMG allows the detection of changes in the electrical activity of the muscle which are typical for each disorder and which might allow a reliable distinction between healthy volunteers and patients with neuromuscular disorders as well as between patients with muscular disorders and patients with neuronal disorders (Figure 3). In contrast to the HSR-EMG of healthy volunteers, the HSR-EMG pattern of patients with neuronal disorders shows high and isolated peaks within the signal course. However, the HSR-EMG pattern of patients with muscular disorders is characterised by low and wide MU action potentials, which are hard to distinguish within the signal course.

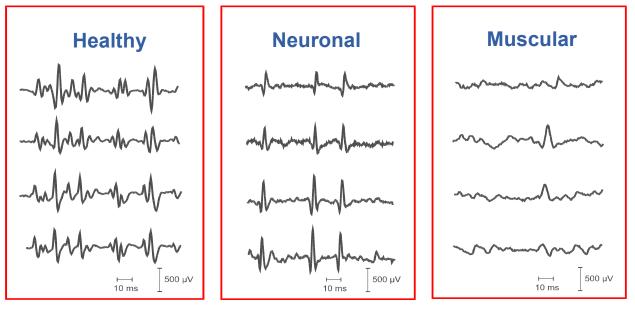


Fig. 3. Pathodological Changes.

Typical pathological changes in the HSR-EMG signal. Represented are four spatially filtered channels.

3. Quantitative evaluation of pathological changes in the HSR-EMG

Due to the first clinical experience with the HSR-EMG the question arises, whether the methodology allows a reliable distinction between healthy volunteers and patients with neuromuscular disorders as well as between patients with muscular disorders and patients

with neuronal disorders. For that purpose a set of parameters has to be introduced, which allow a quantitative evaluation of the changes in the HSR-EMG pattern typical for each disorder. This can be understood as a classical feature extraction process. By an adapted classification procedure, which is based on extracted features, each patient can be assigned to one of the three disorder groups. In this way, the diagnostic selectivity of the noninvasive HSR-EMG can be determined.

Altogether seven parameters have been used for the validation of the typical differences in the HSR-EMG pattern of healthy volunteers, patients with muscular disorders and patients with neuronal disorders. The parameters can be divided into three groups regarding the excitation spread, the entire signal course in time as well as the shape of isolated peaks within the signal [Huppertz 1997]. Most of the parameters are well established in the field of signal processing and data analysis.

3.1 Parameters characterising the HSR-EMG signal in time

This group of parameters describes the entire signal course in time. In this way, the interaction of all MU located within the recording area of the spatial filter is regarded. The parameters belonging to this group are the signal entropy (H), the first zero crossing of the auto-correlation function (ACF_{zero}), the Chi-value (χ) as well as the number of values exceeding the RMS (T_{RMS}).

The signal **entropy (H)** is a parameter well known in the field of signal processing. It describes the relation between the amplitude values of each sample within one measurement. Thus the entropy quantifies the predictability of the next measured amplitude value and characterises, in this way, the stochastic variability of the signal.

$$H = 1 - \sum_{i=\min}^{\max} \frac{p(x_i) \cdot \ln p(x_i)}{\ln(2)}$$

 x_i = measured value

 $p(x_i)$ = occurrence probability of x_i

min = smallest measured value

max = largest measured value

Comparable to the signal entropy the **first zero crossing of the auto-correlation function** (ACF_{zero}) quantifies the stochastic variability of the signal too. The auto-correlation function (ACF) describes how similar different signal parts are. In the case of non-deterministic signals, like the HSR-EMG signal, the first zero crossing takes at higher values place, if the signal becomes more equal to itself.

$$ACF_{zero} = \frac{1}{2T} \sum_{t=-T}^{T} s(t) \cdot s(t+\tau)$$

s(t) = HSR-EMG signal

 τ = time variable

T = smallest measuring duration

t = time

The **Chi-value** (χ) is based on the frequency distribution of the sample values. The frequency corresponds in this case to the probability that a sample with an amplitude within

a given range is appears in the signal. The shape of the frequency distribution can be quantified by means of the χ^2 -test which checks the probability that the frequency distribution is Gaussian. Here, as a quantifying parameter the Chi-value has been introduced. It corresponds not to the probability but to the absolute deviation to a Gaussian distribution.

 $\chi = \sum_{i=1}^{K} \frac{(X_i - N_i)^2}{N_i}$

K = Number of different amplitude values

X_i = Frequency of a certain amplitude in the HSR-EMG signal

N_i = Frequency of a certain amplitude, when a Gaussian distribution is assumed

The parameter values exceeding the RMS (T_{RMS}) has been defined as the number of samples with amplitude higher than the root mean square of the signal. To be independent from the recording time the parameter has been normalised to the total number of samples belonging to the signal.

$$T_{RMS} = \frac{1}{T} \sum_{i=1}^{n} t_i \quad \text{with} \quad \begin{array}{c} t = 1 \quad x_i > RMS \\ t = 0 \quad x_i < RMS \end{array}$$

n = number of samples T = measuring duration t = time

3.2 Parameters regarding the isolated peaks

The excitation of a single MU can be identified in the signal by isolated peaks. Therefore, to the second group belong parameters describing the shape of isolated peaks. A signal part has been identified as a peak, if the following criteria are satisfied:

- The maximum amplitude must be higher than three times the RMS of the signal.
- Between the peak maximum and the adjacent minima the signal has to be continuous increasing respectively decreasing.
- The signal part identified as a peak is limited by the first crossing of the baseline before the minimum left to the peak maximum and by the first zero crossing of the baseline after the minimum right to the peak maximum

In initial investigations it has been shown that two parameters are sufficient to characterise the changes in the HSR-EMG pattern [Huppertz 1997]. These parameters are the **slope of the peak (S)** and the **peak amplitude frequency distribution (PAFD)**.

The parameter **slope of the peak** has been defined as the amplitude difference between the left minimum of the peak and its maximum divided by the time delay between both points. The parameter has been calculated for each peak detected within the HSR-EMG signal. The median value of all slops has been used standing in for all peaks which occur in the signal.

$$S = median \left[\left| \frac{x_{\min} - x_{\max}}{t_{\min} - t_{\max}} \right| \right]_{P}$$

P = number of peaks

The **peak amplitude frequency distribution (PAFD)** counts the number of peaks which have maximum peak amplitude within in a given interval. Similar to the frequency distribution of sample values the peak amplitude frequency distribution corresponds to the probability that a peak with maximum amplitude in a given interval can be found in the HSR-EMG signal. The PAFD of patients with muscular disorders shows high values for low amplitude peaks and low values for high amplitude peaks. This is in contrast to patients with neuronal disorders in which a typical biphasic shape of the PAFD can be found [Ramaekers 1993]. As a parameter describing the shape of the peak frequency distribution, the centroid of area has been calculated. The centroid of area is defined as the amplitude interval which divides the peak frequency distribution in two areas of the same size.

$$\sum_{i=1}^{a-1} N_i \Delta a < \frac{\sum_{i=1}^{A} N_i \Delta a}{2} < \sum_{i=a}^{N} N_i \Delta a$$

 N_i = Frequency of maximum peak amplitudes within the interval i A = Number of intervals Δa = interval width a = PAFD = bound which satisfies the inequality

3.3 Parameters regarding the excitation spread

The most significant parameter describing the excitation spread along the muscle fibres is **the conduction velocity in single MU (MUCV)**. The MUCV can be determined from the delay between the maximum amplitude of one peak in two adjacent and parallel to the muscle fibres orientated channels and their spatial distance (Figure 4). Since the conduction velocity depends on the temperature of the muscle, all MUCV values have been normalised to a temperature of 33°C [Rau 1997]. It has been shown earlier by Ramaekers et al. that the conduction velocity in single MUs is decreased in muscular disorders but unchanged in neuronal disorders [Ramaekers 1993].

3.4 Classification process

The parameter set can be used as a basis for the classification of the patients in healthy volunteers, patients with muscular disorders, and patients with neuronal disorders. Therefore, a classification procedure has been introduced based on a Fuzzy-approach [Kamel 1991].

Since the parameters have different diagnostic selectivity, the classification procedure has to be adapted to this specific classification task. This has been done by introducing weighting factors between 0 and 50 for each parameter. The weighting factors regard the contribution of each parameter to the classification result. They have been optimised by classifying a training data set generated with an especially developed muscle model [Disselhorst-Klug 1998]. This was to separate the training data set from the data set used for validation. The training data set consists of different simulated HSR-EMG signals regarding muscle structures with no pathological changes, muscle structures where a loss of muscle fibres takes place (muscular disorders), and muscle structures where a loss of entire MUs takes place (neuronal disorders) [Disselhorst-Klug 1998].

Performing the Fuzzy classification process, in a first step, all parameter values have been normalized to mean zero and variance 1. Starting the classification process, three clusters have been defined using a hierarchical cluster process like the nearest neighbourhood

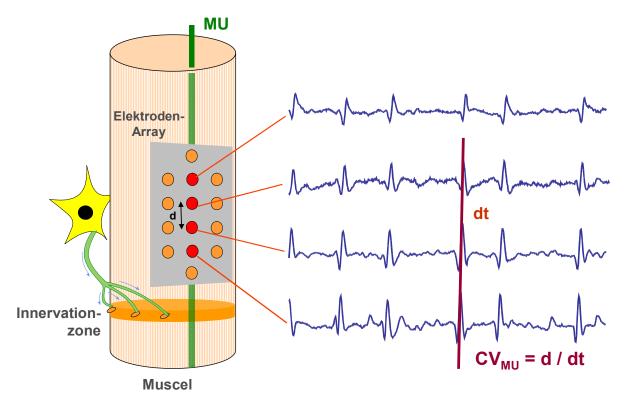
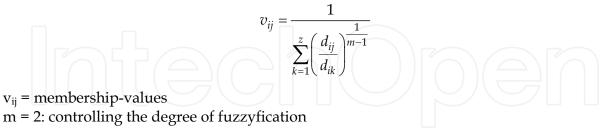


Fig. 4. Conduction velocity.

The conduction velocity of single motor units MUCV can be detected by several NDDfiltered channels arranged parallel to the muscle fibres.

algorithm. These three clusters represent the groups "neuronal disorder", "muscular disorder" and "healthy". The centroid of each cluster has been used to characterise its position in the feature space. After that, the Euclidian distances between the features of each HSR-EMG signal and the centroid of each cluster have been calculated. According to the Fuzzy classification process introduced by Kamel et al. [Kamel 1991], membership-values v_{ij} have been calculated:



d_{ij} = Euclidian distance between the HSR-EMG_i and the centroid of the cluster_j

 d_{ik} = Euclidian distance between the HSR-EMG_i and the centroid of the cluster_k

z = 3: Number of clusters

Afterwards a new centroid for each cluster Z_j has been has been determined following:

$$\vec{Z}_j = \frac{\sum_{i=1}^n v_{ij} \vec{x}_i}{\sum_{i=1}^n v_{ij}}$$

n = 7: Number of parameters

x_i = set of parameter values calculated from the HSR-EMG_i

Due to the weighting of the set of parameter values calculated from the HSR-EMG signals with the membership-values, this iteration converges. The iteration process has been stopped when the following abort criterion is fulfilled:

s = Number of iteration
$$\sum_{j=1}^{z} \sum_{k=0}^{n} \left| Z_{jk}^{(s)} - Z_{jk}^{(s-1)} \right|$$

 $\varepsilon = 0.9$: defined value

Next the membership-ship values have to be normalised with:

$$\overline{v}_{ij} = \frac{v_{ij}}{\sum_{k=1}^{z} v_{ik}}$$

And finally, each HSR-EMG signal has been assigned to the cluster with the highest membership-value.

The training data set, consisting of simulated HSR-EMG signals and representing the different types of disorders, has been classified with all possible combinations of weighting factors. The optimal combination of weighting factors was found when a maximum number of simulated HSR-EMG signals were classified correctly. The weighting factor combination as a result of the optimisation process is shown in Table 1.

Parameter Weighting-factor		
Signal entropy	2	
First zero crossing of ACF	1	
Values exceeding the RMS	19	
Chi-value	19	
Slope of the peak	2	
Peak frequency distribution	9	
MUCV	40	

Table 1. Weighting of the parameter.

Optimised weighting factors for each parameter. The weighting-factors take the diagnostic selectivity of each parameter into consideration. [Disselhorst-Klug 1998]

The same classification algorithm can be used to classify HSR-EMG signals recorded in patients suffering from neuromuscular disorders. Here, in a first step the parameter values have to be multiplied by the related weighting-factor. Afterwards the classification procedure has to be executed as described above.

4. Clinical validation

The HSR-EMG has been recorded at isometric, maximum voluntary contraction of the m. abductor pollicis brevis. The used electrode array consists of 16 gold covered pin electrodes

(0.5 mm diameter) in a two-dimensional arrangement. Due to the low distance between the m. abductor pollicis brevis and the recording side, the inter-electrode distance has been chosen to 2.5 mm. Directly at the electrode array, each of the 16 EMG-leads has been amplified and, later, transmitted to a recording unit. It consists of a band-pass filter (1 – 500 Hz) and a second amplifier. All 16 EMG-leads have been stored on a PC with a sampling frequency of 4000 HZ each. The spatial filtering of the EMG-data has been performed on the PC by specially developed software. From each spatially filtered channel, all evaluation parameters have been calculated. The value of each parameter has been averaged over all NDD-filtered channels. After determination of the parameter values, the HSR-EMG signal of each patient has been assigned to one of the three groups by the described Fuzzy classification process.

For the quantitative evaluation of the typical HSR-EMG patterns altogether 97 subjects, healthy volunteers (41) and patients with neuromuscular disorders (56), aged between the infancy and 25 years, have been investigated. The group of patients investigated consists of 35 patients with Duchenne Muscle Dystrophy (muscular disorder) and 21 patients with Spinal Muscle Atrophy (neuronal disorder). The diagnosis of the patients has been proofed by muscle biopsy. The parameters have been calculated in three different HSR-EMG recordings of each child. Afterwards, the median value of each parameter has been used, accounting for the typical HSR-EMG pattern. Some of the parameters, such as the conduction velocity in single MUs depend significantly on the age of the investigated child [Huppertz 1997]. Those parameters have been normalised to an age of eight.

Diagnostic selectivity of the HSR-EMG: 97%			
	Duchenne	Healthy	SMA
classified as muscular disorder	35	0	0
classified as healthy	0	41	3
classified as neuronal disorder	0	0	18
sensitivity	100%	100%	90%
specificity	100%	95,1%	100%
positive prediction	100%	93,2%	100%

Table 2. Diagnostic selectivity of the non-invasive HSR-EMG in children with Duchenne muscle dystrophy and spinal muscle atrophy. Shown, are the numbers of patients which have been classified in each group. Adapted from [Disselhorst-Klug 2000]

The result of the classification which was based on the weighted evaluation parameters is summarised in Table 2. With the classification, 100% of all investigated healthy children, 100% of all investigated patients with muscular disorders, and 87% of all investigated patients with neuronal disorders have been correctly identified. That mean, that on the average, in 97% of all investigated children the diagnosis by means of the non-invasive HSR-EMG was correct.

5. Conclusions

The High-Spatial-Resolution EMG provides information about the single MU activity in a non-invasive way even during maximum voluntary contraction of the muscle. Therefore,

the methodology could be suitable for a non-invasive diagnosis of neuromuscular disorders. Earlier investigations of healthy children and children with Duchenne Muscle Dystrophy or Spinal Muscle Atrophy have shown, that there is a typical change in the HSR-EMG signal course in each patient group. These typical changes in the HSR-EMG pattern can be evaluated by seven parameters regarding the signal course in time, the shape of isolated peaks, and the excitation spread in single MUs. Based on these evaluation parameters and an especially developed classification procedure, it is possible to classify correctly 97% of all investigated children. That means, in this patient group, the diagnostic selectivity of the HSR-EMG is in the same range or even better than the commonly used needle-EMG techniques. This result could be reached, though the HSR-EMG methodology is limited to superficial muscles and MUs. Therefore, the HSR-EMG promises to be a suitable tool for a non-invasive diagnosis of neuromuscular disorders in clinical application.

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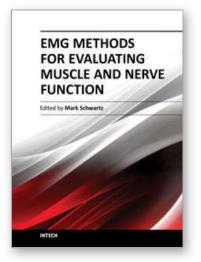
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EMG Methods for Evaluating Muscle and Nerve Function Edited by Mr. Mark Schwartz

ISBN 978-953-307-793-2 Hard cover, 532 pages Publisher InTech Published online 11, January, 2012 Published in print edition January, 2012

This first of two volumes on EMG (Electromyography) covers a wide range of subjects, from Principles and Methods, Signal Processing, Diagnostics, Evoked Potentials, to EMG in combination with other technologies and New Frontiers in Research and Technology. The authors vary in their approach to their subjects, from reviews of the field, to experimental studies with exciting new findings. The authors review the literature related to the use of surface electromyography (SEMG) parameters for measuring muscle function and fatigue to the limitations of different analysis and processing techniques. The final section on new frontiers in research and technology describes new applications where electromyography is employed as a means for humans to control electromechanical systems, water surface electromyography, scanning electromyography, EMG measures in orthodontic appliances, and in the ophthalmological field. These original approaches to the use of EMG measurement provide a bridge to the second volume on clinical applications of EMG.

How to reference

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Catherine Disselhorst-Klug (2012). Non-Invasive Diagnosis of Neuromuscular Disorders by High-Spatial-Resolution-EMG, EMG Methods for Evaluating Muscle and Nerve Function, Mr. Mark Schwartz (Ed.), ISBN: 978-953-307-793-2, InTech, Available from: http://www.intechopen.com/books/emg-methods-for-evaluatingmuscle-and-nerve-function/non-invasive-diagnosis-of-neuromuscular-disorders-by-high-spatial-resolution-emg



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