Investigation of the Relationship between the Amplitude of the Maximum Responses of Compound Muscle Action Potential (CMAP) Scan and the Motor Unit Number Estimates (MUNE)

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***Abstract*— This study intends to exert the liaison between the Motor Unit Number Estimate (MUNE) and the Maximum Response of Compound Muscle Action Potentials (CMAPmax) of the CMAP Scan. MUNE is a neurophysiological method for diagnosing and monitoring Neuromuscular Disorders. CMAP Scan is a technique recording the responses of the gradually stimulated motor neurons. This process eventuates in a Stimulus-Response (SR) curve to monitor the courses of these disorders. Normal cases are demonstrated with a sigmoid curve in this plot. In case of Motor Unit (MU) loss requiring higher stimulus intensities the shape of SR curve gets changed. Therefore, the correlation MUNE with a feature less dependent to the shape of SR curve such as maximum CMAP might be investigated. Materials and Methods: Motor neuron (MN) groups with 5 to 300 axons were formed in a simulation software and they were stimulated by currents incrementally from 0 to 99 mA. The CMAPs which are the peak-to-peak voltage amplitudes (V_{pp}) of the waveforms of CMAP traces are the responses to these currents in SR Curve. The maximum CMAP (CMAPmax) being the highest amplitudes of responses were found for each MN group. The coefficient of determination and the Pearson correlation coefficient between MU number and the maximum CMAP were found as 0.9976 and 0.999 respectively. This suggests a linear relationship between MU number and maximum CMAP. The maximum CMAP can be suggested as a new feature in building new mathematical models.**

Keywords*— *Compound Muscle Action Potential (CMAP) Scan; Motor Unit Number Estimate (MUNE); Neuromuscular Diseases; Stimulus-Response (SR) Curve; Motor Unit Action Potential (MUAP), Maximal Compound Muscle Action Potential (CMAPmax)

I. INTRODUCTION

Motor Unit Number Estimation (MUNE) is a quantitative method that is exploited to determine the number of axons representing the MU number approximately as precisely as possible. These values serve to assess MU losses in monitoring neuromuscular disorders [1]. This method is performed by applying currents as stimulus in gradually increased intensities to a motor neuron and by recording the responses of the muscles increased by this nerve to these stimuli as Motor Unit Action Potentials (MUAPs) [2-3].

Compound Muscle Action Potential Scan (CMAP Scan) is an electrophysiological method employed for diagnosing neuromuscular diseases. The responses of the muscles innervated by gradually stimulated motor neurons are recorded and then graphically represented as Stimulus-Response (SR) Curve [4-5]. This is shown in Figure 1. Despite the problems, associated with interindividual variability, CMAP amplitude is commonly accepted as a measure of the number of intact MUs in theory [6]. Some studies were previously conducted utilizing CMAP Scan for MUNE [7]. Maximal CMAP ($CMAP_{max}$) is the amplitudes of responses which no longer increase even though repeated stimuli are applied at supramaximal levels [6]. $CMAP_{max}$ can be assumed that this represents the recruitment of entire MUs [8].

In this sense, the aim of the study is to investigate the liaison between the motor unit number estimates (MUNE) and the Maximum Response of CMAP ($CMAP_{max}$) of the CMAP Scan.

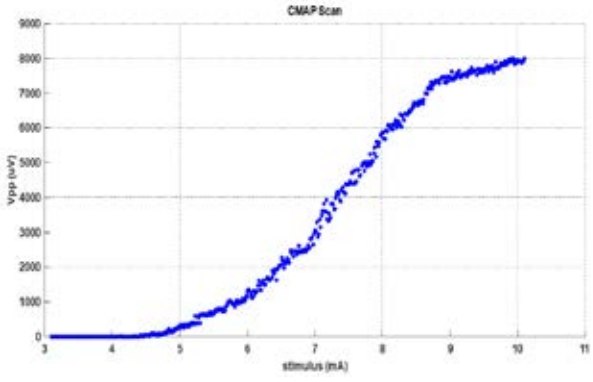

Fig 1. The CMAP Scan (SR curve) of a healthy individual (stimulus in mA vs number of axons in μV

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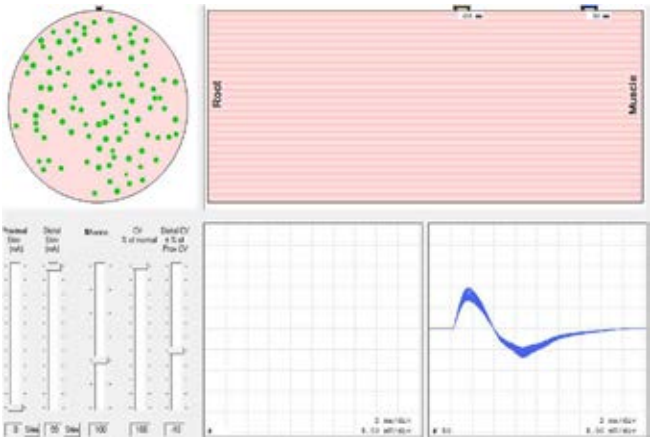

Fig 2. Gradual incremental stimulation of the Motor Neuron and the CMAP responses in the Simulator.

There are previous studies presenting Mean Slope of SR Curve and Total Slope of SR Curve as features in computing MUNE [9-10]. Therefore, $CMAP_{max}$ might be also suggested another feature for this purpose.

II. Materials and Methods

A. Building Data Sets

The data sets were built through a simulator software ((Motor Nerve Conduction Studies (MNCS) Neurography Simulator version 2.4, Keypoint Club, Uppsala, Sweden) by creating motor neuron groups comprising 5 to 300 axons. Currents lying between 0 to 99 mA with increments of 1 mA were used to stimulate each of these groups. The waveforms of the CMAP traces are demonstrated via the interface of the simulator which is shown in Figure 2. The data concerning the numerical values of these traces were stored in a folder in ".txt" format in the root directory of the computer through "export" menu of the simulator. Data analysis was achieved by processing the data by a MATLAB Code.

B. Compution of $CMAP_{max}$

The responses are the peak-to-peak amplitude values of CMAP traces (V^{pp}) which are the response of all stimuli. It is expressed as follows;

$$V_{PP}(i) = CMAP(i) = V_{max}(i) + |V_{min}(i)| \quad (1)$$

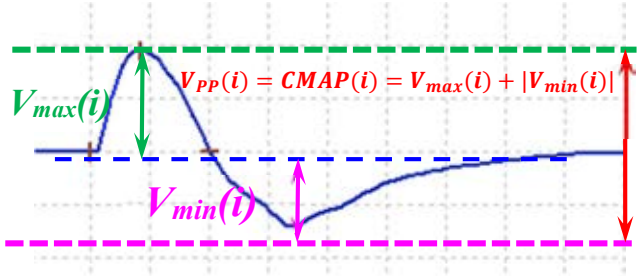

Fig 3. The peak-to-peak representation of CMAP

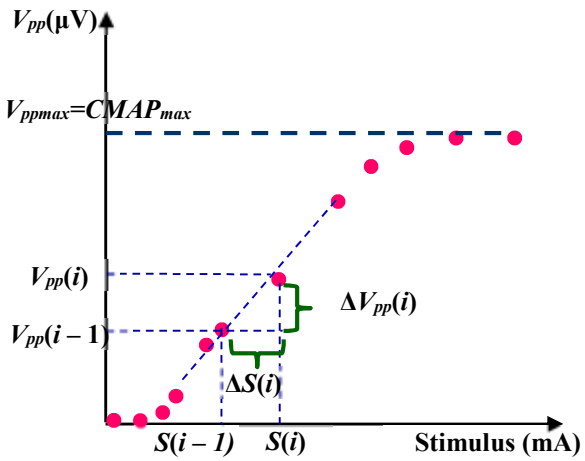

Fig 4. CMAPmax in Stimulus-Response (SR) Curve

where $V_{max}(i)$ is the maximum value of the CMAP trace and $V_{min}(i)$ is the minimum value of this trace. The graphical representation of the CMAP is shown in Figure 3.

So the maximum value of CMAPs in SR-Curve is demonstrated as follows;

$$CMAP_{max} = V_{ppmax} = max[V_{pp}(i)] \quad (2)$$

where V_{ppmax} is the maximum value of the responses. The $CMAP_{max}$ in SR Curve is illustrated in Figure 4.

C. Program Codes for Computations

A MATLAB® (Version R2015a) (Mathworks, USA) Code was formed to process the exported data in ".txt" format from the simulator. The peak-to-peak voltages (CMAPs) of each CMAP traces corresponding to each stimulus and the maximum of value of these voltages were computed through this code. The Flow Chart of this code is represented in Figure 5.

D. Statistical Analysis of the Data

The relationship between the Number of MUs and the maximum CMAP values was studied by computing the correlation coefficient. SPSS Software Package (IBM® SPSS Statistics® v.22.0, SPSS, Inc., Chicago, IL) was employed for this statistical analysis.

III. Results and Discussion

The $CMAP_{max}$ values calculated from the CMAP Scan data generated by the simulation software are presented in terms of MU in Table 1.

Furthermore, the plot of $CMAP_{max}$ vs the MU numbers is shown in Figure 6.

In Figure 6, the fact that the majority of the data are concentrated in the vicinity of a regression line is remarkable. Besides, the Coefficient of Determination was found as 0.9976 (R^2=0.9976).

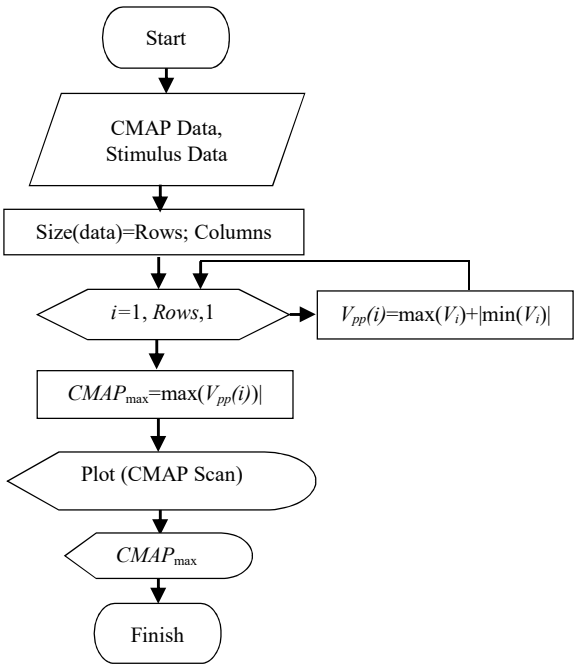

Fig 5. The Flow-Chart of the Program Code for computing the Total Slope

The relationship between the MU numbers (Number of Axons) and the maximum CMAP was analyzed statistically and the Pearson Correlation Coefficient was found as 0.999 (ρ=0.999).

The simulator used in this study does not enable the users to form pathological states. Therefore, the effects of disorders progressing with axon loss on the parameter tackled in this study were not studied. Nevertheless, the maximum CMAP and the simulated MU number in cases of pathology can be done in simulators allowing to create these conditions.

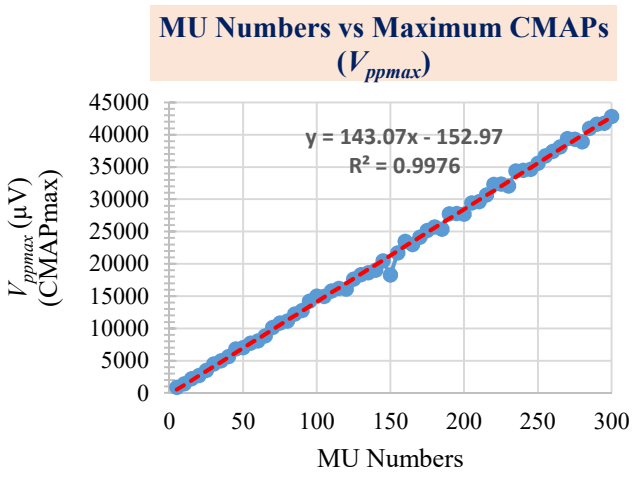

Fig 6. The plot of the relationship between maximum CMAPs and MU numbers (number of axons.)

TABLE 1. MAXIMUM CMAPS AND MU NUMBERS

Number of Simulated Axons (n_{axon})(Numbers of MUs)	$CMAP_{max}$ Values
5	849.6 ± 364.24
10	1385.8 ± 245.37
15	2188.8 ± 502.92
20	2685.4 ± 343.94
25	3507 ± 244.47
30	4477.4 ± 883.71
35	4982.4 ± 669.14
40	5628.4 ± 397.30
45	6810.8 ± 769.55
50	7027.4 ± 889.72
55	7715.4 ± 475.36
60	8032.8 ± 874.39
65	8835 ± 1183.22
70	10157.2 ± 1218.27
75	10848.4 ± 588.03
80	11106.6 ± 291.40
85	12226.4 ± 1276.23
90	12785 ± 1241.53
95	14204.2 ± 693.81
100	14984.8 ± 1093.70
105	14969.4 ± 900.44
110	15809.8 ± 1419.88
115	16208.4 ± 584.44
120	16084.2 ± 712.16
125	17618.4 ± 105.44
130	18304 ± 0.00
135	18613 ± 0.00
140	19017 ± 0.00
145	20462.4 ± 808.68
150	18273 ± 0.00
155	21684.8 ± 1664.14
160	23495.8 ± 1224.53
165	22963.2 ± 807.19
170	24109.8 ± 2726.71
175	25161 ± 971.85
180	25683.6 ± 702.80
185	25350.8 ± 1559.05
190	27748.4 ± 740.88
195	27781.8 ± 1615.09
200	27667.6 ± 1604.381
205	29423.6 ± 2604.22
210	29613.4 ± 1456.20
215	30666 ± 1406.62
220	32322.4 ± 1321.79
225	32364.8 ± 1700.79
230	32065 ± 968.62
235	34366 ± 1879.31
240	34481.4 ± 1866.11
245	34628.2 ± 2287.60
250	35600 ± 1838.78
255	36692.2 ± 2096.25
260	37387.8 ± 1102.50
265	38118.2 ± 690.40
270	39370.8 ± 1155.81
275	39303.6 ± 1857.77
280	38887.4 ± 2249.01
285	40956 ± 1510.06
290	41626 ± 1563.86
295	41778 ± 1050.05
300	42827.2 ± 2129.97

TABLE 2. PEARSON CORRELATIONS BETWEEN MAXIMUM CMAPS AND MU NUMBERS IN SPSS®

	Motor Unit (MU) Number	CMAPmax
Motor Unit (MU) Number	1	0.999 ($p < 0.0001$)
CMAPmax	0.999 ($p < 0.0001$)	1

The result of the statistical analysis in terms of Pearson Correlation between Motor Unit (MU) Number and the maximum Compound Muscle Action Potential ($CMAP_{max}$) is represented in Table 2. This result supports the linear relationship between these variables

Moreover, MUs exhibit more stochastic neurophysiological characteristics in disease conditions leading the relationship between maximum CMAP and the MU numbers to deviate from linearity.

IV. CONCLUSIONS AND RECOMMENDATIONS

From Figure 6, it might be observed that low maximum CMAP values are related with low MU numbers. Low MU numbers may be due to either the MU losses resulting from the neuromuscular pathologies or the structural and functional characteristics of certain muscles. The relationship between maximum compound muscle action potential (CMAPmax) of the CMAP scan and the motor unit (MU) number (number of axons) is found to be linear. As a result, it was found that maximum CMAP can be regarded as a feature in monitoring MU loss during the progress of neuromuscular diseases, and can be used in building mathematical models.

In conclusion, maximum CMAP ($CMAP_{max}$) may be taken into account as one of the features that were studied in previous studies in building mathematical models as the basis of MUNE methods [9-10].

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