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Assessment of neuromuscular electrical stimulation effect on contralateral quadriceps muscle

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ABSTRACT

Background: In the field of rehabilitation, the acute application of neuromuscular electrical stimulation (NMES) causes not only peripheral muscle contraction but also involve the central nervous system by the transient increase in spinal motor neuron and cortical activity. Therefore it has been used in several fields of rehabilitation. Previous studies used surface electromyography to assess this effect. But we conducted our study to assess the effect of NMES on contralateral quadriceps muscle in normal individuals using another method needle electromyography.
Methods: A study carried out on 20 normal males, who were subjected to (i) NMES Training Program for 60 min for the right quadriceps muscle. (ii) Assessment of EMG activity for rectus femoris muscle (RF) on the contralateral side. An assessment was done for minimal volition and maximal volition or interference pattern analysis, this assessment was done twice: before the start of NMES and during the session.
Results: EMG of voluntary activity (Minimal volition) and Maximum voluntary activity analysis for RF muscles showed increased duration (in millisecond), amplitude (in millivolt) ($P < 0.01$), increased activity in turn per second, amplitude/turn (M) (uV) compared to the result before NMES application.
Conclusion: Our study provides a new evident date that the acute NMES application to the contralateral quadriceps muscles, leads to significant facilitation of the maximal voluntary power in the ipsilateral muscles through activation of efferent neural control. This facilitating effect of motor neurons in the contralateral muscles is likely due to the complex combination interaction between spinal and supraspinal control.
Trial registration: Trial registration: PACTR202010887172053.

1. Background

Neuromuscular electrical stimulation (NMES), a widely used rehabilitation modality, leads to neuromuscular system contraction using electrical current (**Maddocks et al 2013**; **De Oliveira et al 2013**). In the field of rehabilitation, the acute NMES application causes not only peripheral muscle contraction but also involves the central nervous system by the transient increase in spinal motor neuron response and cortical activity (**Bergquist et al 2011**;**Liu et al 2020**), which significantly improves muscle power and physical function (**Annette et al 2017**). In addition, various studies showed that NMES directly facilitates the healing process in the corticospinal tract (CST) (**Chen et al 2014**; **Jang et al 2014**; **Jang and Seo 2018**).

Later, it was found that unilateral voluntary muscle contraction in one limb induces complex changes in the motor pathways controlling the other side. (**Zijdewind and Kernell 2001**; **Hordacre and Perrey 2020**).

Recently, several studies on NMES showed that electric stimulation for one limb, has improved the contralateral muscle strength, which occurred by activating the contralateral motor pathway, contralateral hemisphere, and the ipsilateral sensory or motor cortical areas (**Arkov et al 2010**;**Kadri et al 2017**; **Minetto et al 2018**; **Cattagnia et al., 2018**). These finding show that the unilateral motor and sensory activity affect structures bilaterally producing cross education or neural adaptation (**Green and Gabriel 2018**), which are relatively dependent on direct or indirect corticospinal projections(**Hendy and Lamon 2017**).

However nearly all of these studies assessed the muscles using

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surface electromyography (SEMG). Although it is an important tool in muscle assessment, there is a limitation in the extracted information from the signal, e.g., the EMG amplitude which is influenced by the electrode location, subcutaneous tissue thickness, conduction velocities, motor unit (MU) distribution, and the detector system used. In addition there is crosstalk that is a signal recorded by one muscle which is actually generated by a nearby muscle. The same with amplitude cancellation and amplitude changes which underestimates the changes in MU activity when there is a modulation in muscle strength. Recently, there has been debate on the effect of rectification on EMG spectral analysis and coherence measure **(Farina et al 2004, 2014)**. In this context, **Del Vecchio et al in 2017** have clarified that the spectral properties of the SEMG was not reliably correlated with the MU recruitment.

On the other hand there is the needle EMG (NEMG) which is less affected by crosstalk and provides greater accuracy and repeatability, and it can record low threshold, and small MUs missed by SEMG, moreover it can assess the discharge properties of motor neurons originating in the spinal cord (**Carroll et al 2011**; **Selvanayagam et al 2012**). It evaluates the MUs by assessing the motor unit action potential (MUAP) voluntary contraction (amplitude, duration and Area). The amplitude is calculated as the maximum amplitude between the positive and negative peaks of the main spikes. The duration is the time from the initial deflection until the signal returns to the baseline, reflecting the activity of muscle fibers within 2.5 mm of the electrode tip (**Preston and Shapiro 2012**; **Tsao 2021**). In addition, the interference pattern as regard turns/second (T/S) and amplitude which depends on MUAPs summation and recruitment, in which the number of turns is influenced by the number of MUs and their rate of firing (**Kimura 2001**).

Therefore, the study was performed to assess the effect of NMES on contralateral quadriceps muscle in normal individuals using needle EMG, to find out if the minimal and maximal volition values show significant change before and after NMES? Our study differed from others (**Howard and Enoka 1991**; **Minetto et al 2018**; **Cattagnia et al., 2018**), who used surface EMG to detect the NMES effect. Since no other studies were done on the effect of NMES using NEMG, we had to compare our study with those using surface SEMG.

2. Methods

2.1. Study design

This study was approved by the FMASU Research Ethics Committee (R 59/2020) and was registered at Pan African Clinical Trial Registry with a registration number of PACTR202010887172053. All patients understood the procedure and signed written informed consent.

2.2. Participants

From October to December 2020, 30 age matched male subjects were recruited in the outpatient clinic of the Physical medicine, Rheumatology and Rehabilitation Department of the authors' institution, 21 normal male individuals were selected according to the inclusion criteria, 9 were excluded due to the presence of medical illness, of which 20 completed the study as one of them had abnormal EMG finding (neuropathy).

The inclusion criteria were: adult males, their ages ranged from 20 to 45 years old, free of any chronic medical illness, with no previous experience with NMES.

We also excluded patients who have any cardiovascular, musculoskeletal or neurological disorders.

All patients underwent a full history taking with particular emphasis on any pre-existing medical condition, and clinical examination to rule out any medical condition.

2.3. Study interventions

All interventions were performed at the Department of Physical Medicine and Rehabilitation by two specialized physiatrists who are experts in these procedures (one worked for the EMG study and the other for the NMES program). All the interventions were performed in the same setting for around 90 min.

All subjects were subjected to (i) NMES Training Program for 60 min on the right quadriceps, (ii) Assessment of EMG activity for rectus femoris (RF) muscle on the left side, (which was done twice: before and during the NMES program).

2.4. Outcome measures

The outcome measures are the EMG data before and during the NMES program for the contralateral muscle.

2.5. The procedure

- ❖ Participants were seated in an upright position, their trunk at 0° in respect to the vertical position, and their knee joints nearly 100°–110° (180°:is the knee in full extension (**De Ruiter et al 2006**) **.**
- ❖ Participants had one session that lasted for approximately 90 min has occurred in the following sequence:

  1-After a standardized warm-up for both quadriceps muscles.

  2 Before NEMG recording of the left quadriceps muscle, each subject was instructed to practice each maximal voluntary contraction MVCs of the left quadriceps muscle (extension against the resistance of the physicians). All subjects were given consistent verbal encouragement during the maximal excursion. The trial lasted for 5 s and was repeated three times with 3 min of rest between each MVCs trial (for normalization purposes) before NEMG recording.

  3-NMES was delivered to the right RF and current intensity was adjusted to the tolerated level by the participants.

  4-Participants were asked to perform 3 trials of left RF MVCs (for normalization purposes) then another NEMG recoding to the left RF while the right RF receiving NMES.

2.5.1. NMES training program

NMES was delivered using Pagani apparatus (Master 932, Electronica, Italy) using four adhesive rubber electrodes (6 × 4 cm) which gives biphasic square pulses symmetrical in a frequency of 50 Hz for 400 μs, for the right quadriceps muscle motor points. The on-off ratio was set to 5:10 s, and the ramp-up and downtimes adjusted to 1 s for 60 min. The intensity was set as the accepted level by participant causing muscle contraction with Mean ± SD (29.25 ± 5.7 mA) (**Cattagnia et al 2018**).

2.5.2. Assessment of EMG activity

The EMG activity of (RF), muscle on the other contralateral side (left side) was recorded using NEMG (Deymed Diagnostic, True Trace EMG, Czech), disposable concentric needle 50mm × 0.45 mm (2'' × 26G) was used, insertion was at 4 finger-breadth proximal to the upper pole of the patella for RF and the ground electrode at the knee joint (**Preston and Shapiro 2012**). The assessment was done for minimal volition for about 20 MUAPs and maximal volition or interference pattern analysis which was set at sensitivity 1mv/

division and the sweep speed 200 ms/division, and the electromyographic software calculated the amplitude/turn (M) (μV), turns/second (T) (Hz) and the M/T ratio (%) automatically.

This assessment was done twice the first before the start of NMES and the second time was during the session.

2.6. Sample size

This study aimed to assess the effect of NMES on contralateral quadriceps muscle in normal individuals using NEMG. Based on a previous study by Minetto et al., 2018 who investigated that increases in voluntary activation during NMES was +5.7%. To achieve a 95% confidence level and a margin of error of 10%, a minimum sample size of 21 will be needed for a single proportion using the large sample normal approximation. Sample size estimation was performed by Raosoft statistical package.

2.7. Statistical analysis

Data were collected, revised, coded and entered to the Statistical Package for Social Science (Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, New York: IBM Corporation). The quantitative data were presented as mean, standard deviations and ranges when parametric, and median, inter-quartile range (IQR) when data found non-parametric. The comparison between non parametric variables before and after the use of NMES was done using Wilcoxon Rank test. The confidence interval was set to 95%; so, the p-value was considered significant at the level of <0.05.

3. Results

This study was a study on 21 healthy men, where one of them didn't complete the study because of abnormal EMG finding (neuropathy) and we resumed with twenty persons, their ages Mean ± SD were 31 ± 6.4 yrs. All of them were free from any cardiac, musculoskeletal system or neurological disease and volunteered for participation in this study. No one of them had back experience with the NMES (Table 1).

3.1. Results of needle EMG for minimal voluntary activity

EMG for Minimal volition before and during NMES for the left Rectus femoris muscle showed increased duration from (12.04–12.9), amplitude increased from (826.5–1150.5) and area from (1333–1667) where (P value < 0.01) showing highly significant difference in all of them(**Table 2**).

3.2. Results of needle EMG for maximal voluntary activity (interference pattern analysis) before and after NMES

For maximal volition showed increased activity in turn per second from (426–653) and amplitude/turn from (340–537) with (P value < 0.01) showing highly significant difference in both of them (Table 3) (Figs. 1 and 2).

Table 1
Demographic data of participants.

No. (20 male)	Mean ± SD	Range
Age (Years)	31.50 ± 6.39	21–45
Height (cm)	173.2 ± 6.43	165–182
Weight (kg)	74.40 ± 2.22	68–80

4. Discussion

Neuromuscular electrical stimulation (NMES), a widely used rehabilitative method that uses electrical current to cause neuromuscular system contraction (**Maddocks et al 2013**). Several studies showed that NMES directly facilitates the healing process in the CST (**Chen et al 2014;Jang and Seo 2018; Zheng et al 2018**). Later, it was found that unilateral voluntary muscle contraction in one limb induces complex changes in the motor pathways controlling the other side (**Zijdewind & Kernell, 2001; Hordacre and Perrey 2020**).

The current study was conducted to assess the effect of NMES on contralateral quadriceps muscle in normal individuals using NEMG to find out evident and accurate data. Our study was different from others, who used SEMG to detect this NMES effect. Since no other studies were done on the effect of NMES using NEMG, we had to compare our study with those using SEMG.

The main Results in our study: 1- Before and during NMES, NEMG for voluntary activity (minimal volition) on the contralateral side exhibited an increase in duration from 12.04 to 12.9 ms, amplitude from 826.5 to 1150.5 mv, and area from 1333 to 1667, showing highly significant difference in all of them.2**-** NEMG for maximal voluntary activity (interference pattern analysis) showed increased activity in turn per second 426 to 653, and amplitude/turn from 340 to 537 μV showing a highly significant difference.

The results indicated an increase in contralateral muscle strength, which agrees with other studies (**Arkov et al 2010; Kadri et al 2017; Minetto et al 2018**; **Cattagnia et al., 2018**). Where **Kadri et al 2017** assessed a training program for 8 weeks either with NMES, or exercise and found an increase in MVC of the ipsi and contralateral limbs equally.

While **Cattagnia et al., 2018** stated that, the acute NMES application for the right quadriceps increased the MVC torque by 4–5% for the left knee extensors using SEMG. The same with **Minetto et al (2018)** who investigated that a single session of unilateral application of NMES or focal vibration to the quadriceps muscle increased the neural drive and MVC torque in the contralateral muscle using SEMG.

On the other hand the study done by **Jang and Seo (2018)** was different from ours. Although they found facilitation of the contralateral CST, but with no improvement of fine motor activity after 2 weeks of NMES training on peripheral hand muscles in normal subjects, but this study assessment method was hand function only without EMG to detect the changes inside the muscles.

Similarly with Howard and Enoka (1991) study to determine whether the bilateral deficit is due to neural mechanisms. All subjects produced an increase in the maximal voluntary left leg force during right leg electro-stimulation. Although the changes in electromyogram did not completely correspond the changes in force; however they did not give too much emphasis to these EMG findings (as this was beyond the scope of their study) and they didn't obtain the surface EMG amplitude, or the voluntary activation.

According to previous studies that used SEMG for assessment (**Howard and Enoka 1991**; **Minetto et al 2018; Cattagnia et al., 2018**) which has a lot of limitations like the EMG amplitude which is influenced by the electrode location, subcutaneous tissues thickness, distribution of MU conduction velocities and the detection system, furthermore there is crosstalk, amplitude cancellation and amplitude changes which underestimates the changes in MU activity(**Farina et al 2004; Farina et al 2014; Del Vecchio et al in 2017**) and that was evident in the results of the previous studies which had no definite values for amplitude, duration or interference pattern analysis that caused limitations in these studies.

Table 2
Comparison for EMG voluntary activation (Minimal volition) before and after the use of NMES.

Minimal volition		Before	After	Test value•	P-value	Sig.
		No. = 20	No. = 20			
Duration	Median (IQR)	12.04 (11–13)	12.9 (12.04–14.0)	−3.403	0.003	HS
	Range	10–15	12–16			
Amplitude	Median (IQR)	826.5 (631–1033)	1150.5 (907–1242)	−5.477	0.0001	HS
	Range	567–1230	690–1427			
Area	Median (IQR)	1333 (944–1540)	1667 (1238–2284.5)	−4.335	0.0001	HS
	Range	848–1935	1025–2609			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant HS) •: Wilcoxon Rank test.

Table 3
Comparison of EMG of the Maximum voluntary activation (Interference pattern) before and after the use of NMES.

Interference pattern		Before	After	Test value ‡	P-value	Sig.
		No. = 20	No. = 20			
Turns	Median (IQR)	426 (322.5–455)	653 (556–727.5)	−3.922	0.0001	HS
	Range	254–650	500–2515			
Amplitude	Median (IQR)	340 (293–414)	537 (443–823)	−3.734	0.0001	HS
	Range	255–478	300–4541			

P-value > 0.05: Non significant (NS); P-value < 0.05: Significant (S); P-value < 0.01: highly significant (HS)‡: Wilcoxon Rank test.

Fig. 1. An image for maximum voluntary activity (interference pattern)
For rectus femoris muscle before NMES showing normal turns and amplitude for the candidate. (Turns: 470 HZ, Amp: 313uv).

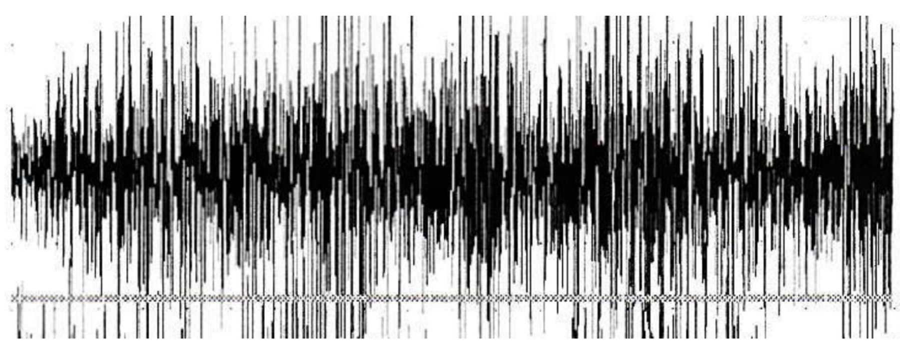

Fig. 2. An image for maximum voluntary activity (interference pattern)
For rectus femoris muscle after NMES showing increased turns and amplitude for the candidate. (Turns: 724 HZ, Amp: 824uv).

Therefore, we conducted our study using needle NEMG to avoid most of these limitations in SEMG and to induce accurate results for the change inside the muscle, where it can record low threshold and small MUs missed by SEMG, in addition it assess discharge properties of motor neurons originating in the spinal cord (**Carroll et al 2011**; **Selvanayagam et al 2012**), by the parameters of voluntary contraction (amplitude, duration and Area) and Interference pattern as regards T/S and amplitude.

The number of turns and T/S increase as the force of contraction increase (**Pan et al 2015**), while the recruitment of motor units is reflected as increased amplitudes of the signal spikes (**Nandedkar et al 1998**; Potvin and Fuglevand, 2017**)**. The voluntary contractions (amplitude, duration and area) reflect the degree of motor unit activation; the higher amplitudes reflect an increased rate of motor units discharge or a higher number of recruited MUs (**Gazzoni et al 2004**).

Our results could be explained from the neurophysiological image; that this facilitation in the MVC power and the efferent neural pathway occurred by the contralateral NMES could be the result of crossed excitatory effects occurring at multiple levels in the neural pathway (**Kadri et al 2017**; **Cattagnia et al., 2018**). The same was proved by **Jang & Seo in** 2018 who showed facilitation of the contralateral corticospinal tract (CST) after two weeks of NMES training of the peripheral muscles in normal candidates.

Also the integration of the skin mechanoreceptors, cutaneous reflexes, free nerve endings or nociceptors have a facilitator effect on the motor neurons innervation of the contralateral identical muscles (**Gueugneau et al 2017**). Moreover, **Kato et al. (2019)** found that the spinal reflex excitability that leads to Inter-limb facilitatory effect depends not only on the induction of central orders from the cortex but also on peripheral input induced by muscle contraction by using NMES. Therefore, there is an interaction between the afferent inputs to the spinal cord, the descending motor command, and the sensorimotor cortical areas occurring with unilateral NMES (**Ruddy et al 2017**; **Cattagnia et al., 2018**).

4.1. The implications of the current study

We can use it in rehabilitation practice where unilateral voluntary contraction is difficult either: uncomfortable, painful or not accessible (after surgical intervention, bracing, burn or nerve repair) to avoid the disuse atrophy. Furthermore, the fact that approximately all candidates cannot perform their maximal power with a unilateral isometric contraction.

This study has some limitations as follows: 1) EMG activity was recorded from only RF muscle, while not for vastus medialis or lateralis muscles, in which its activity may have provided more help to complete the picture of contralateral NMES effects. But we were using NEMG which is more uncomfortable.2) the small number of study subjects.3) dealing with only male subjects.

5. Conclusion

Our study provides evident date that the acute NMES application to the contralateral quadriceps muscles, leads to significant facilitation of the maximal voluntary power in the ipsilateral muscles by activating its efferent neural control. This facilitated effect of the motor neuron in the contralateral muscles is likely due to the complex combination interaction between the spinal and the supraspinal control.

Ethics approval and consent to participate

This study was approved by Ain Shams University, Faculty of Medicine Research Ethics Committee (REC) FWA 000017585. FMASU R 59/2020.

A written informed consent was obtained from patients sharing in the study.

Consent for publication

A written consent was taken from the patients and available upon request.

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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CRediT authorship contribution statement

Hala M.Abd Elsabour Sabah: Formal analysis, Data curation, Writing – original draft, Writing – review & editing, Contribution to design of the work; clinical work, interpretation of data; the acquisition, analysis, and interpretation of data; and revision. has drafted the work and substantively revised it. Preparation, writing, review and editing of manuscript and statistical data. Approved the submitted version. Agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work. **Hossam salaheldin Abdelmohsen Labib:** Conceptualization, Formal analysis, Data curation, Writing – original draft.

Declaration of competing interest

The authors declare no conflict of interest and no funding received.

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