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Association between psychosocial factors and dose of neuromuscular electrical stimulation in subjects with rheumatoid arthritis[1]

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Abstract.
BACKGROUND: The therapeutic effect of neuromuscular electrical stimulation (NMES) on muscle strengthening and hypertrophy depends on its dose. Patients must tolerate high doses of NMES to maximize gains in muscle function. It is unknown why some patients are able to achieve high NMES dose while others are not. Disability and psychological attributes may play a role in a patient's tolerance of NMES dose.
PURPOSE: To explore if disability and psychological attributes associate with the ability to achieve high doses of NMES in patients with rheumatoid arthritis (RA).
METHODS: Cross-sectional study. Forty subjects with RA participated in 2 sessions of NMES intervention to the quadriceps muscles. The highest NMES dose achieved by each subject was recorded. Dose was defined as the torque produced by the NMES as a percentage of the torque produced during a maximum voluntary isometric contraction. Subjects were then grouped in high or low NMES dose. Variables investigated in this study included disability, pain coping strategies, pain acceptance, sense of mastery or control, anxiety, and depression. Correlations were sought between these factors and NMES dose.
MAIN RESULTS: In unadjusted models, disability, coping self-statements, catastrophizing, and anxiety were predictors of NMES dose. In adjusted models only disability (OR = 0.17 [95% CI: 0.04, 0.77]) and catastrophizing (OR = 0.85 [95% CI: 0.72, 0.99]) predicted NMES dose.
CONCLUSION: Patients with RA with lower disability and lower catastrophising achieve higher doses of NMES. Identifying factors associated with achieving high NMES dose may guide strategies to improve effectiveness of this intervention.

Keywords: Muscle function, electrical stimulation, NMES, tolerance, dose

1. Introduction

Neuromuscular electrical stimulation (NMES) is an intervention commonly used in rehabilitation settings that has been shown to increase muscle strength, reverse muscle atrophy, and improve physical

[1]Study performed by the Department of Physical Therapy, University of Pittsburgh.

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function in a variety of patient populations [1, 2]. As the effectiveness of NMES is equivalent to that of voluntary exercise, NMES appears particularly helpful in patients who cannot perform voluntary exercise at sufficiently high doses to promote therapeutic effects, such as patients with chronic rheumatic, heart and lung diseases in which NMES has demonstrated beneficial effects [3–6].

The effectiveness of NMES appears to follow a dose-response curve; i.e., the larger the dose, the larger the therapeutic gains [7–9]. NMES dose is normally defined as the magnitude of torque produced by the electrically elicited muscle contraction expressed as a percentage of the torque produced during the patient's maximum voluntary isometric muscle contraction (MVIC) [1, 10]. Thus, to maximize gains in strength and muscle mass, patients should endure high doses of NMES. Yet, a disadvantage of NMES is that its electrical stimulation can be noxious. The higher the dose, the more noxious the electrical stimulus. While NMES has been shown to be generally well tolerated [1], some patients are unable to tolerate the discomfort associated with achieving high doses of NMES [11]. Therefore, intolerance or inability to achieve higher doses of NMES can be a barrier to its effective use in clinical practice.

Several factors may contribute to the patient's ability to achieve high doses of NMES. Among these factors, the patient's level of disability and psychological attributes related to pain perception such as coping strategies [12, 13], pain acceptance [14], sense of control over life [15–18], depression [19] and anxiety [20] may all play a role. Our interest in these factors is grounded on empirical observations during the application of NMES in daily practice. For example, we have observed that the more anxious patients, those with low sense of control over their lives, and patients with higher depressive symptoms do not seem to tolerate NMES well; whereas patients able to distract themselves from the noxious electrical stimulus seem to achieve higher doses of NMES. However, these empirical observations have not been examined. Studies on NMES have mainly focused on the investigation of stimulation parameters and waveforms related to NMES tolerance [21–25]. Identifying psychosocial factors related to the ability to achieve high doses of NMES could have important implications for selecting patients that can benefit most from this intervention and for developing strategies to increase patients' tolerance to higher doses of NMES, ultimately maximizing the benefit from NMES intervention.

Patients with rheumatologic diseases such as rheumatoid arthritis (RA) are a suitable patient population to examine factors related to NMES tolerance for several reasons. Firstly, muscle weakness is present in more than 50% of patients with RA and is generally accompanied by muscle atrophy [26, 27], justifying NMES as an intervention for these patients. Secondly, patients with RA seem to respond favorably to NMES. In a small study in RA, NMES was found to contribute to increasing muscle strength and cross-sectional area, and the patients who tolerated higher NMES doses experienced larger benefits [11]. Thirdly, patients with RA experience significant functional limitations and NMES can be a viable alternative for the most disabled patients who have difficulty performing voluntary exercises at sufficient intensity to reverse muscle weakness and atrophy. Finally, patients with RA tend to be more affected by psychological factors than healthy adults and may provide a wide range of these attributes in order to test the association with NMES dose [28–30].

The purpose of this study was to explore psychosocial factors (disability and psychological attributes) associated with the ability to achieve high doses of NMES in patients with RA. We hypothesized that subjects with low levels of disability, anxiety and depression, and high levels of pain acceptance, sense of personal mastery, and adaptive pain coping strategies would be more likely to tolerate higher NMES doses.

2. Methods

This was a prospective, correlational, cross-sectional study that took place in the laboratory of the Physical Therapy Department at University of Pittsburgh, PA, USA. It was approved by the University of Pittsburgh Institutional Review Board (IRB). All participants in this study signed an informed consent document approved by this IRB. The procedures followed during the study were in accordance with the Helsinki Declaration of 1975, as revised in 1983 [31].

2.1. Subjects

Participants were included if they were older than 21 years and had a diagnosis of RA by a rheumatologist

according to the Criteria of the American College of Rheumatology [32]. Participants had to be able to ambulate independently to ensure their safety while partaking in the study. Their RA medication regimen had to be stable for at least 1 month prior to treatment. Exclusion criteria were a history of a neurological or musculoskeletal disorder that affected muscle function, prior quadriceps tendon or patellar tendon rupture, a previous adverse reaction associated with electrical stimulation treatment, history of cardiovascular disease or unstable hypertension, surgery to the dominant lower extremity within the past six months, or current use of statin medication. We did not include patients with passive knee flexion range of motion less than 70° because they would not have been able to perform the quadriceps torque testing procedure.

Participants were recruited from the University of Pittsburgh Medical Center's Arthritis Registry. Approximately 1,200 letters were sent out to participants of the registry. We received 62 calls from individuals inquiring about the study. To achieve the target sample size of 40 we screened 53 subjects over the phone. From these, 8 declined participation and 5 were not eligible, leaving 40 eligible subjects.

2.2. Procedures

Subjects attended two testing sessions, 5 to 9 days apart. During the first session, demographic data on age, gender, ethnicity, BMI, marital status, and education were collected along with biomedical data such as duration of RA disease and RA medications. These data were collected to characterize the sample and to explore the need to control for these variables during data analysis. Patients also completed self-reported questionnaires related to disability and psychological factors followed by the NMES protocol. During the second session, subjects participated in the NMES protocol only.

2.2.1. Self-reported questionnaires

The Health Assessment Questionnaire Disability Index (HAQ-DI) was used to assess disability due to RA. The disability index is expressed on a scale from 0 – 3 where 0 indicates no functional disability and 3 indicates severe functional disability [33]. The HAQ-DI is a valid measure of disability in RA, and its test-retest correlations have ranged from 0.87 to 0.99 [34, 35].

To quantify pain coping strategy, we used the Coping Strategies Questionnaire (CSQ). The CSQ measures eight coping categories: diverting attention, reinterpreting pain sensation, coping self-statements, ignoring pain sensation, praying or hoping, catastrophizing, increasing activity level, and increasing pain behavior. Each category is comprised of the sum of 6 items, with scores ranging from 0 to 36. Higher scores represent greater reliance on that coping strategy to decrease pain. The CSQ has good internal consistency (Cronbach's alphas from 0.71 to 0.85) and validity [36, 37].

The Chronic Pain Acceptance Questionnaire (CPAQ) was used to measure two domains of chronic pain acceptance: activity engagement and pain willingness. Activity engagement evaluates the patient's participation in activities while recognizing if pain is present [38]. Pain willingness determines the degree to which a patient allows pain in an experience without using efforts to avoid and/or control it [38]. Maximum score for activity engagement is 66 while for pain willingness it is 54. Higher scores represent greater pain acceptance. Individuals who exhibit higher levels of pain acceptance are more likely to experience adaptively response to pain [14]. The CPAQ has been found to have reasonable reliability (r from 0.59 to 0.76) [14, 39].

The Sense of Mastery Scale (SMA) was used to measure patient's sense of control over their life and environment. The SMA scores range from 7 to 28. Low scores represent low sense of control over their life and environment [40]. It was demonstrated that individuals who feel they have more control over their life and environment adjust to both psychological and physical pain better than those who feel they have less control [15–18]. The SMA has been validated against measures of mental and physical health [40–42].

Subjects' depressive symptoms were measured using the Center for Epidemiological Studies Short Depression Scale (CESD). CESD scores range from 0 to 30. Higher scores represent more depressive symptoms. It was demonstrated that depressed individuals tend to have lower pain tolerance than the non-depressed ones [19]. The CESD has good internal consistency (Cronbach's alpha from 0.85 to 0.90 across studies) and validity [43, 44].

The Anxiety Inventory Form (AI) is a short version of the well-validated Spielberger's State-Trait Personality Inventory [45]. The AI scores range from 10 to 40. Higher scores represent higher levels of anxiety. It was demonstrated that anxious individuals with

chronic pain are more likely to experience further pain and negative effects, which could affect their tolerance to the noxious NMES [20].

2.2.2. NMES protocol

The NMES protocol was repeated during two sessions 5 to 9 days apart. These choices were based on our clinical experience. Two sessions were preferred rather than one as it takes a couple of sessions for patients to adapt and feel comfortable with the electrical stimulus. In addition, more than two sessions was not deemed necessary because while NMES doses tend to increase somewhat over several sessions of intervention, usually the final dose is not far from the dose achieved after the initial two sessions. At least 5 days between sessions was needed to provide enough time for the muscle to recover. The protocol was administered by the same clinician and included testing the strength of the quadriceps muscles followed by 15 NMES contractions.

Both strength testing and NMES intervention were administered as is regularly done in clinical practice. The maximum volitional isometric contraction (MVIC) test was used to determine the strength of the quadriceps muscles in order to set-up the NMES dose. For the strength test, subjects were seated on an isokinetic dynamometer (Biodex System 3 Pro, Shirley, NY) with the knee at 70 degrees of flexion. Subject position, stabilization, and gravity correction were performed according to the Biodex manufacturer's guidelines. Subjects exerted as much force as possible while trying to extend the knee against the force arm of the dynamometer positioned in the distal aspect of the anterior leg (just above intermalleolar line). Each MVIC contraction was 3 to 5 seconds long. The MVIC was the highest torque output (Nm) of four trials [46]. Strong verbal encouragement from the tester and visual feedback from the dynamometer screen was provided during trials. We have demonstrated good intra- and inter-tester reliability for this test procedure in our laboratory (ICC = 0.97 and 0.82, respectively, data not published).

After determining the MVIC, the NMES was administered as we usually do in clinical practice. Subjects were seated on the dynamometer in the same position as for the quadriceps strength test. An Infinity Plus portable NMES unit (Empi, 599 Cardigan Road, St. Paul, MN) was used to deliver the electrical stimulation. The Infinity Plus produces a constant current with a peak output of 100 mA, a programmable pulse duration of 50 to 450 microseconds, and utilizes a symmetrical biphasic waveform. The stimulus parameters included a pulse rate of 75 pulses/second and pulse duration of 450 microseconds. The stimulus parameters used in this study have been shown to maximize force output in previous studies [47, 48]. Stimulus on/off time settings were 14 sec on (4 sec ramp up, 6 sec full contraction, 4 sec ramp down), and 46 seconds off to minimize muscle fatigue during the intervention (1-min cycle). Ramps 4 seconds long were used to maximize patient's comfort. Six seconds of full contraction is in line with the time used by several studies on NMES [1]. The skin areas where the electrodes were applied were rubbed with alcohol. Two 6.9 cm by 12.7 cm self-adhesive electrodes (Dura-Stick, Chattanooga Corp., Chattanooga, TN, USA) were placed on the thigh, one proximal over the muscle belly of the vastus lateralis and one distal over the muscle belly of the vastus medialis as previously described [11].

Participants were instructed to relax and allow the NMES to produce the muscle contraction. Utilization of NMES administration without voluntary activation of the quadriceps muscles has been used at least twice as often in research studies than NMES combined with voluntary muscle activation [1]. During NMES application we offered verbal encouragement and assurance regarding the safety of the procedure. A total of 15 electrically elicited contractions were applied. The intensity of the NMES was gradually increased as tolerated during the session.

Torque data from the dynamometer was transferred to a second computer in which a custom-made program using LabVIEW software (National Instruments, Austin, TX) was used for data processing. The computer screen from the LabVIEW software displayed a marker with the MVIC torque value that was used to encourage higher tolerance to the NMES intervention. We recorded the intensity of the NMES device along with the NMES dose during each NMES contraction. The highest NMES dose during the 2 testing sessions was used in the analysis.

NMES dose was the outcome of this study. NMES dose was defined as the torque produced by the electrically elicited muscle contraction expressed as a percentage of the torque during the MVIC (NMES torque/ MVIC torque). NMES dose was categorized as "high NMES dose" or "low NMES dose". To be classified as a "high NMES dose", subjects had to have achieved a NMES dose of 50% of MVIC or higher. The reasons to choose high dose at 50% of MVIC were

threefold. A literature review of NMES has shown that 50% of MVIC is above the level that has been used by most studies [10]. Several experts in NMES have suggested that 50% of MVIC appear to be an adequate dose for NMES quadriceps femoris muscle training [49, 50]. One study compared doses above 50% to doses below 25% and reported significant improvement in muscle strength favoring the high dose [51].

2.3. Data analysis

The study was designed to have 40 participants. Forty subjects would provide 80 percent power, one-sided test, type I error of 0.05, to detect a small univariate association ($r = 0.37$) between each independent and the dependent variable. Forty subjects would be adequate for our planned logistic regression based on 2 variables in each regression model (one control variable and one predictor variable) considering a 50% rate of subjects (20 subjects) achieving high NMES dose. This assumes that approximately 10 subjects in the high NMES dose group are necessary to supply statistical power for each variable entered into the logistic regression.

Our analytical strategy was to test the associations between disability and psychosocial factors and NMES dose. For that, descriptive statistics were calculated for the demographic, disability and psychological factors with respect to subjects who achieved or did not achieve high doses of NMES (50% of MVIC). Means and standard deviations or medians and ranges were used to describe continuous variables with and without normal distribution respectively, whereas frequency and percentage were used to describe categorical variables. Independent *t*-tests were performed to examine group differences in NMES doses for continuous normally distributed variables, independent samples Mann Whitney U tests were used for continuous non-normally distributed variables, and chi-square tests were used for categorical variables. The factors that reached statistical significance were used to build logistic regression models.

The association of disability, and psychological factor with NMES dose was examined in separate unadjusted logistic regression models. Those significant univariate associations were then included in a multivariate logistic regression adjusted for demographic factors meeting this criterion. The regression analyses were referenced such that higher Odds Ratios indicate a higher likelihood of achieving high NMES dose. The significance level for all analyses was $p < 0.05$. IBM SPSS statistical software version 20 was used for calculations.

3. Results

From the 40 eligible subjects, two did not complete the second session resulting in 38 subjects. Despite multiple attempts, contact with one subject was lost after the first session. The other subject complained of intense muscle pain after the first visit and did not want to repeat the NMES intervention within the protocol timeframe.

The average dose (% of MVIC) for the high NMES dose group was $62.8 \pm 10.5\%$ whereas for the low NMES dose group it was $29.8 \pm 14.3\%$ (difference of 33%, $p < 0.0001$). Information on demographics, disability and psychological factor variables between high NMES dose and low NMES dose groups is provided in Table 1. The demographic characteristics between high versus low NMES dose were similar except for BMI which was lower for subjects in the high NMES dose group. Group differences were observed for disability, coping self-statements, catastrophizing, and anxiety, with the high NMES dose group demonstrating less disability, catastrophizing and anxiety; and greater coping self-statements. The other variables were not associated with NMES dose.

Table 2 provides the summary of the logistic regression analyses results. In unadjusted models, disability, coping self-statements, catastrophizing, and anxiety were all significant predictors of NMES dose. BMI was the only demographic factor related to NMES dose and therefore was controlled in the adjusted regression models. Disability and catastrophizing were significant predictors of NMES dose in both the unadjusted and adjusted models. For each level of reduction in disability, subjects had an 83% increase in odds of achieving high dose of NMES. For each level of reduction in catastrophizing, subjects had a 15% increase in odds of achieving high dose of NMES.

4. Discussion

To the best of our knowledge, this is the first study to investigate psychosocial factors related to achieving high doses of NMES. The main finding of this study is that subjects with lower disability and lower

Table 1
Subject characteristics with respect to NMES dose. Data represent means and standard deviations unless otherwise stated

	Low NMES Dose $N=16$	High NMES Dose $N=22$	P value
Demographics			
Age	60.8 ± 10.8	59.1 ± 11.4	0.663
Gender- *n* of females (%)	9 (56)	15 (68)	0.452
Education in years- median (Q25, Q75)	14.0 (12.0, 17.0)	16.0 (14.0, 18.2)	0.069
Body Mass Index (BMI) in Kg/m^2	30.9 ± 7.4	26.1 ± 5.3	0.026
Ethnicity- *n* of white (%)	11 (69)	20 (91)	0.082
Marital Status- *n* married (%)	8 (50)	13 (59)	0.983
Disease Duration in years- median (Q25, Q75)	14.0 (8.0, 24.0)	16.0 (11.0, 21.0)	0.529
Medication – *n* using (%):			
NSAID	11 (69)	18 (82)	0.350
Opioid	3 (19)	3 (14)	0.670
DMARD	13 (81)	17 (77)	0.767
Steroid	7 (44)	6 (27)	0.290
Disability and Psychological Factors			
Disability† - median (Q25, Q75)	1.12 (0.40, 1.40)	0.13 (0.00, 0.91)	0.007
Coping Strategies‡:			
Diverting attention	18.1 ± 8.7	17.4 ± 7.7	0.803
Reinterpreting Pain Sensation	11.1 ± 8.3	8.5 ± 5.9	0.261
Coping Self Statements	23.9 ± 5.4	28.1 ± 6.0	0.034
Ignoring Pain Sensation	15.9 ± 7.8	18.0 ± 8.7	0.443
Praying & Hoping	18.7 ± 9.2	16.9 ± 7.7	0.518
Catastrophizing	8.9 ± 4.7	5.3 ± 4.5	0.022
Increasing Activity Level	21.0 ± 6.1	21.2 ± 7.4	0.923
Increase Pain Behaviors	23.0 ± 4.8	22.5 ± 4.4	0.766
Chronic Pain Acceptance¶:			
Activity Engagement	43.7 ± 10.8	49.8 ± 8.7	0.063
Pain Willingness- median (Q25, Q75)	25.0 (21.0, 39.0)	27.0 (23.0, 36.0)	0.596
Sense of Mastery^	21.7 ± 2.5	23.1 ± 3.4	0.189
Anxiety§	19.5 ± 5.4	15.6 ± 5.5	0.037
Depression$^+$ - median (Q25, Q75)	6.5 (3.0, 10.0)	3.0 (2.0, 6.0)	0.060

NSAID = non-steroidal anti-inflammatory drug; DMARD = disease-modifying anti-rheumatic drug; †determined by Health Assessment Questionnaire; ‡determined by Coping Strategy Questionnaire; ¶determined by Chronic Pain Acceptance Questionnaire; ^ determined by Sense of Mastery Scale; §determined by Anxiety Inventory Form; $^+$ determined by Epidemiological Studies Depression Scale.

Table 2
Odds of achieving high doses of NMES for disability, coping self statements, catastrophising, and anxiety

	Unadjusted OR (95% CI)	Adjusted OR^ (95% CI)	Nagelkerke^ R^2
Disability†	0.15 (0.04, 0.62)*	0.17 (0.04, 0.77)*	0.39
Coping Self Statements‡	1.14 (1.00, 1.29)*	1.12 (0.98, 1.28)	0.26
Catastrophizing‡	0.84 (0.73, 0.98)*	0.85 (0.72, 0.99)*	0.30
Anxiety§	0.88 (0.77, 0.99)*	0.90 (0.79, 1.03)	0.25

^ Models adjusted for BMI; *significance level $p \leq 0.05$; †determined by Health Assessment Questionnaire; ‡determined by Coping Strategy Questionnaire; §determined by Anxiety Inventory Form.

catastrophizing are more likely to achieve high doses of NMES. Findings may suggest that to improve the effectiveness of NMES, subjects with higher level of disability should receive special consideration when administering NMES treatment. Findings may also indicate that the utilization of strategies to decrease catastrophizing may result in higher NMES dose and more effective muscle strengthening and hypertrophy.

The finding that more disabled subjects are less likely to achieve higher doses of NMES supports our hypothesis and is in agreement with the literature that has demonstrated a link between disability and pain acceptance. Yet, this finding is somewhat discouraging since the more disabled patients are the ideal popula-

tion for NMES intervention as they may not be able to perform voluntary exercise at high enough doses to promote therapeutic benefits. Hence, more disabled patients with RA likely require additional strategies to help them cope with high NMES doses. Such strategies could include providing additional information about the NMES procedure, educating the patients on the potential benefits of NMES, coaching towards achieving high NMES dose, and distracting the patients so that they do not pay as much attention to the electrical stimulation. We caution that these proposed strategies are not based on research but rather have been the ones we use in clinical practice and appear to help patients to achieve high NMES dose. Another consideration is that more disabled patients may need more time to adapt to the electrical stimulus and additional sessions of NMES are perhaps needed to get them up to a more therapeutic dose.

Catastrophizing was the only psychological attribute that predicted NMES dose. Catastrophizing is a negative coping strategy that reflects the interpretations and reactions to chronic pain rather than the severity of the pain itself. It is the tendency to focus on pain and magnifying, even dramatizing, the possible negative consequences of pain [52]. Studies have demonstrated that catastrophizing is associated with higher pain severity in patients with RA [53–55]. Catastrophizers tend to pay excessive attention to pain and experience more difficulty suppressing pain-related stimuli than do non-catastrophizers [56]. As coping with pain and discomfort, such as during the application of NMES, is a process of adapting to pain by regulating emotional responses to the situation [36, 57], catastrophizers are less likely to tolerate high NMES dose possibly because they are unable to regulate their emotions and suppress the discomfort generated by the NMES.

It has been suggested that to build up patients' pain tolerance either the elimination of negative coping strategies such as catastrophizing or the utilization of positive coping strategies such as ignoring pain sensation could be used [12, 58]. Although we are unaware of treatment paradigms to help patients coping with high NMES dose, in patients with chronic pain cognitive behavioral interventions aimed at increasing the patient's use of positive coping skills have shown to decrease the pain experience and catastrophizing [59–61]. In combat athletes, a study demonstrated that the more the athletes ignore pain, the more they are able to maintain their sport involvement despite their pain [62]. In the context of NMES administration, we propose that cognitive therapy could be attempted by replacing catastrophizing thought with more realistic ones. For example, thoughts such as "The NMES discomfort is terrible and I feel like it's never going to get any better" or "I feel I can't stand it anymore" may be replaced with "As bad as the NMES discomfort gets there are things I can do to make it at least a little better". In addition, a number of behavioral techniques used in chronic pain could also be attempted to increase tolerance to NMES such as using graded exposure to the NMES protocol (initiating NMES then slowly increasing dose) and activity pacing (remaining constant dose when patients feel discouraged and increasing dose on days patients feel good). Studies are warranted to investigate if the suggested intervention strategies would help promoting high NMES dose.

The finding that subjects with lower BMI are more likely to achieve higher doses of NMES, although not part of our research aim, warrants further discussion. BMI explained 20% of variability in NMES dose (Odds Ratio of 0.88, 95% CI: 0.78, 0.99, *data not reported*), indicating that for each level of BMI reduction subjects had a 12% increase in odds of achieving high dose of NMES. This finding is in line with the frequent clinical observation that more obese subjects have difficulty attaining high doses of NMES. While it is intuitive to assume that this observation is due to increased electrical resistance of thicker layer of skin-subcutaneous fat that impede the electrical current to produce strong muscle contractions, this assumption has not been tested before. The implication of this finding is that if one wants to achieve high doses of NMES, the inclusion of obese individuals should be carefully considered since they may not achieve doses of NMES high enough to optimize improvements in muscle strength and hypertrophy.

Limitations of this study include the cross-sectional design and relative small sample. Although we acknowledge that correlational analyses cannot be used to prove causality, they can be used to distinguish variables more likely to impact the NMES dose and to identify factors to be examined in future studies. While the sample is relatively small, the study was adequately powered to run the logistic regressions with two variables per model. Another consideration is that low variability in certain predictors may have accounted for some negative findings. For example, average depression measures were low and might explain the lack of association between depression and NMES dose. Nevertheless, the sample seems to be an adequate

representation of patients with RA since the demographic and biomedical characteristics of our subjects are comparable to the ones reported in other studies in RA [11, 26]. Last, while we consistently asked the subjects to relax the quadriceps muscles, it is uncertain if this strategy has prevented the subjects from carrying out a voluntary contraction along with the NMES.

In conclusion, the results of this study indicate that patients with lower disability and catastrophizing achieve higher doses of NMES. Longitudinal larger studies are necessary to determine if strategies to decrease catastrophising or if special management of subjects with higher disability may help patients to achieve higher doses of NMES and maximize the therapeutic benefits of this intervention. Studies should also continue to investigate the parameters and method of delivery of NMES to make it more comfortable for the patients.

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