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Abstract: *This study aimed to examine the treatment efficacy of noninvasive neuromuscular stimulation, specifically cumulative charge activation technology (CCAT) by (1) quantifying healing responses of musculoskeletal tissues experiencing DOMS post-eccentric exercise; and (2) quantifying symptoms of delayed-onset muscle soreness (DOMS) in treatment versus control groups.*
Untrained, healthy subjects (n=24) were randomly assigned to treatment and control groups and performed an eccentric exercise protocol designed to elicit a DOMS response in elbow flexor muscles. The Control group recovered without post-exercise treatment; while the Treatment group received 5 treatments of CCAT (using the Sigma Q® Bioneuro system) at 2 hours, 1, 2, 4 and 8 days post-exercise. Outcome measures collected to measure tissue damage and healing responses included: serum Creatine Kinase (CK) levels, relaxed elbow angle (REA), and maximum voluntary isometric contractions (MVICs). A survey was used to obtain subjective symptoms before and after exercise in both groups. ANOVA with repeated measures and linear regression techniques were used to examine objective and subjective outcomes.
The recovery slope of the REA in linear regression model was significantly different from zero (T=2.92, p<0.01) and almost twice as great as the Control group's (T=1.39, p=0.169). Serum CK levels and MVICs were significantly associated with Day (p<0.05), but not Treatment (p > 0.05) effects. Self-reported soreness/stiffness of the exercised arm (p<0.001) and arm pain (p<0.05) demonstrated a Treatment x Day interaction, and simple main effects demonstrated decreased symptoms for the Treatment group on certain days.
CONCLUSION: Treatment with Sigma Q® Bioneuro-based CCAT was associated with reduced symptoms of stiffness/soreness and pain, and increased rate of recovery of REA.

Keywords: *Muscle Soreness, Cumulative Charge, Neuromuscular, Pain management, Activation Technology*

Introduction

Individuals exposed to bouts of eccentric muscle exercise experience a short-term inflammatory response (peaking 1 to 3 days post-exercise) that is healed over the period of 1 to 2 weeks.[1 2] This phenomenon is known as Delayed Onset Muscle Soreness (DOMS).[3 4] The development of DOMS is due to the strain experienced by the muscle-tendon unit during eccentric contractions, which causes muscle fibers to incur damage generally in the vicinity of the myotendinous junction. Exposure to such loading conditions typically results in pain, soreness and tenderness, and a significant decrease in force production capacity (thought to be due to sarcomere "popping "and disorganization).[1] DOMS appears to be associated with damage to several structures, including muscle fibers,[3] the sarcoplasmic reticulum[4] and connective tissue.[5] Individuals who experience DOMS due to repeated eccentric contractions appear to subsequently enjoy a training benefit (a resistance to damage from similar eccentric exertions) that may last up to 6 months. This is sometimes referred to as the "repeated bouts effect".[6]
Various techniques have been suggested in attempt to relieve the symptoms of DOMS, or to decrease required healing time.[5] These have included various stretching regimens (pre- and/or post-exercise),[7 8] use of non-steroidal anti-inflammatory drugs,[9-11] and ice-packs and massage treatments to name a few.[12 13 19] However, relatively little evidence exists to support the use of such techniques.
Another method that has gained interest in relieving symptoms and potentially improving the healing process is the use of electrical stimulation therapies. The best-known technique has been referred to as transcutaneous electrical nerve stimulation (TENS), or the topical application of variable voltage pulses via skin electrodes with lower frequency levels, often producing a mild pricking sensation. This technique has been widely used by physical therapists, chiropractors, and others primarily as a treatment to control pain[14] and as an attempt to increase the rate of healing.[15] While the use of TENS has shown to be of benefit in the treatment of certain conditions,[16] such treatment by itself or in combination with cold therapy does not appear to have been effective with respect to DOMS.[17 19]

In this study, the authors sought to examine the efficacy of a new technique of neuromuscular activation in the treatment of DOMS with the Sigma Q® Bioneuro System (Biosysco Holdings Limited, London, UK). Though similar in topical electrode placement as the TENS technique, the Sigma Q® system differs by applying a high-frequency variable voltage series of pulses that produces a cumulative charge and activates neuromuscular deep-tissue muscle contraction. This cumulative charge activation technology

(CCAT) is applied to activate muscle recovery and enhance performance. In published clinical case studies with neuromuscular injury patients, application of this system has demonstrated a marked improvement in patient mobility, lessening of pain, and enhanced rehabilitation[18]. While this previous evidence suggests a therapeutic effect, additional research was needed to assess efficacy of this technology in reducing symptoms and facilitating the healing process. Accordingly, the aim of this study was to evaluate whether treatment with CCAT was effective in reducing objective injury measures and subjective pain symptomatology following exposure to an eccentric exercise protocol designed to elicit a DOMS response.

Methods

All procedures used in this investigation were reviewed and approved by Institutional Review Board (IRB). Twelve males and twelve females (24 volunteers total), in the age range of 19 to 30 years, were recruited in accordance with the IRB process, i.e. participants were required to meet inclusion and exclusion criteria to be eligible for the study. Subject demographic data are presented in Table 1. All subjects were in good general health and were required to provide informed consent prior to participation. Subjects who had engaged in eccentric weight training within the prior 6 months or with prior history of arm pain, breathing problems, blood conditions, or other discomfort with phlebotomy procedures were excluded from study participation. Subjects were financially compensated for their participation.

Table 1. Subject Demographic Data

	Overall			Male			Female		
Demographic Data	**Mean**	**SD**	**Range**	**Mean**	**SD**	**Range**	**Mean**	**SD**	**Range**
Age (years)	25	3	(20, 30)	27	2.2	(22, 28)	24	2.8	(20, 29)
Height (m)	170	9.2	(154, 189)	177	6.8	(167.7, 189.0)	164	5.2	(154.0, 173.5)
Body Mass (kg)	164	43	(46.49, 112.49)	193	38	(55.79, 112.49)	134	22	(46.49, 77.34)
BMI (kg/m^{-2})	25	4.6	(18.50, 32.89)	28	4.4	(19.84, 32.89)	23	3.2	(18.50, 28.41)

CCAT TREATMENT SETUP

The CCAT treatment was administered using the Sigma Q® Bioneuro cumulative charge activation device (Figure 1) and active (50mm x 50mm) electrode connectors (Figure 2). This device is an analog-based, multifunctional device designed to be adjustable for timed therapy sessions. There are four output modes. These include combinations of two rhythm generators and wave signal indicators based on positive or negative polarity.

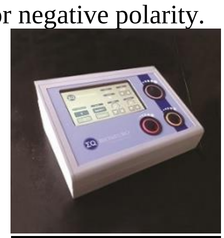

Figure 1. Bioneuro® Unit

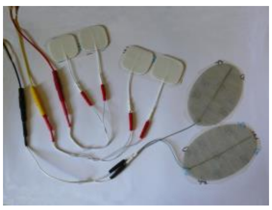

Figure 2. Connecting wires and electrodes

Twenty-four subjects were randomly assigned to either an experimental group or a no-treatment control group. Both groups were exposed to an eccentric exercise regimen designed to elicit DOMS on Day 0 of the experiment. The treatment group was provided five Sigma Q® treatments subsequent to administration of the eccentric exercise. These treatments were administered on Day 0 (4 hours post exercise), and on Days 1 through 4 of the 8-day recovery period. The control group was allowed to recover normally (i.e., no treatment was provided). Dependent measures for this study included: 1) subjective responses collected on a wellness questionnaire that included items assessing symptoms and sleep quality; 2) resting elbow angle (a measure of the severity of the DOMS response; 3) serum creatine kinase (a measure of muscle damage); and 4) maximum voluntary isometric contractions (a measure of the damage and recovery of muscles subsequent to eccentric exercise). Independent variables included Group (treatment versus control) and Day (of post-DOMS recovery period). Statistical analysis procedures included analysis of variance (ANOVA) with repeated measures and linear and non-linear regression methods.

Results

OBJECTIVE OUTCOMES

Maximum Isometric Voluntary Contraction

A significant Day and Gender interaction ($F_{5,\ 100}=4.229$, $p=0.0016$) was observed from the 3-way ANOVA examining factors Treatment, Gender, Day, and interactions. Comparing the 2 genders on individual days, male's MIVCs were significantly greater than female's on all days (Day 0 PRE: p=0.0015; Day 0 POST: p=0.0048; Day 1: p=0.0044; Day 2: p=0.0074; Day 4: p=0.0023; Day 8: p=0.0008). Comparing each gender's MVICs over time, male's MIVCs on Day 0 pre-exercise were significantly greater than Days 0

Figure 6. Average REA on (A) Day 0 was 154.5 degrees, and on (B) Day 2 was 158.0 degrees.

post-exercise (p=0.0002), 1 (p=0.0096), and 2 (p=0.0212); male's MVICs on Day 8 were significantly greater than Days 0 post-exercise (p=0.0002), 1 (p=0.0003) and 2 (p=0.0013). Female's MIVCs on Day 0 pre-exercise were significantly greater than Days 0 post-exercise (p<0.0001), 1 (p<0.0001), and 8 (p=0.0037); female's MIVCs on Day 0 post-exercise were significantly lower than Days 2 (p=0.0432), 4 (p=0.0016), and 8 (p<0.0001) (Figure 7A). Overall, MIVCs on Day 0 pre-exercise were significantly greater than days 0 post-exercise (p<0.0001), 1 (p<0.0001) and 2 (p=0.0013); MIVCs on Day 1 were significantly lower than days 4 (p=0.0005) and 8 (p<0.0001); MIVCs on Day 2 were significantly lower than Days 4 (p=0.0032) and 8 (p<0.0001); MIVCs on Day 4 were significantly lower than Day 8 (p=0.0068) (Figure 7B).

Relaxed Elbow Angle

ANOVA results indicated that Day had a significant effect on REAs (F5, 100=20.20, p<0.0001). A trending effect of Day and Gender was observed (F5, 100=2.017, p=0.0826). None of the pairwise comparisons between males and females on individual days was significant. (Figure 7D). The rate of recovery of REA from Day 0 (post-exercise) through Day 8 for both Treatment and Control groups was examined using linear regression. For the Control group, the equation obtained was:

$$\text{REA (degrees)} = 152.1 + 0.2995 * \text{Day}$$

whose slope was not significantly different from zero. Linear regression analysis for the Treatment group generated the following equation:

$$\text{REA (degrees)} = 152.4 + 0.5607 * \text{Day}$$

with a significant slope ($p = 0.0049$). The coefficients of these equations indicate that starting from approximately the same resting elbow angle on Day 0 post-exercise, the treatment group REA recovered at approximately twice the rate of recovery of that experienced by the control group (Figure 7C).

Creatine Kinase
Gender significantly affected CK levels from the results of the 3-way ANOVA ($F_{1, 20}=8.791$, $p=0.0077$). Day was a significant factor ($F_{1, 22}=9.240$, $p=0.0060$) when non-significant terms were pooled with error. On Day 1, males' CK was significantly greater than females' ($p=0.0177$) (Figure 7E, F).

SUBJECTIVE OUTCOMES
Results of subject perceptions of soreness/stiffness (Figure 8A) from 3-way ANOVA demonstrated a significant interaction of Treatment and Day ($F_{5, 100}=7.738$, $p < 0.0001$). Subject reports of Arm Pain also exhibited a significant Treatment by Day interaction ($F_{5,100}=2.56$, $p=0.032$), as shown in Figure 8B.

Subjects' perceived limitations in work and daily activities demonstrated a significant Day effect ($F_{5, 100}=8.143$, $p < 0.0001$) and trending Treatment by Day interaction ($F_{5, 100}=1.940$, $p=0.0943$) and Gender * Day interaction ($F_{5, 100}=1.924$, $p=0.0970$) effects. In the Control group, the rating was significantly lower on Day 0 than Days 1 ($p=0.0282$), 2 ($p=0.0282$), and 4 ($p=0.0463$); Day 8's rating was significantly lower than Days 1 ($p=0.0176$), 2 ($p=0.0176$) and 4 ($p=0.0146$). Finally, subject assessment of sleep quality was found not to be affected by any of the independent variables ($p > 0.05$).

Discussion

Results of this study suggest that the treatment with CCAT demonstrated beneficial effects in both objective and subjective outcomes. Results of the regression analyses of the recovery of the relaxed elbow angle in the treatment and control groups showed a significant slope in REA recovery for the treatment group, but not for the control group. REA is thought to be due to an influx of calcium from the damaged sarcoplasmic reticulum and appears to be indicative of the amount of damage sustained by the affected muscle due to eccentric contractions[4]. Results showing that the treatment groups experienced a faster recovery of the baseline relaxed elbow angle, suggest the possibility that repair to the sarcoplasmic reticulum may be enhanced as a result of the treatments provided. Further research may be necessary to verify this possibility. However, no treatment effects were observed for recovery of isometric strength or expression of CK.

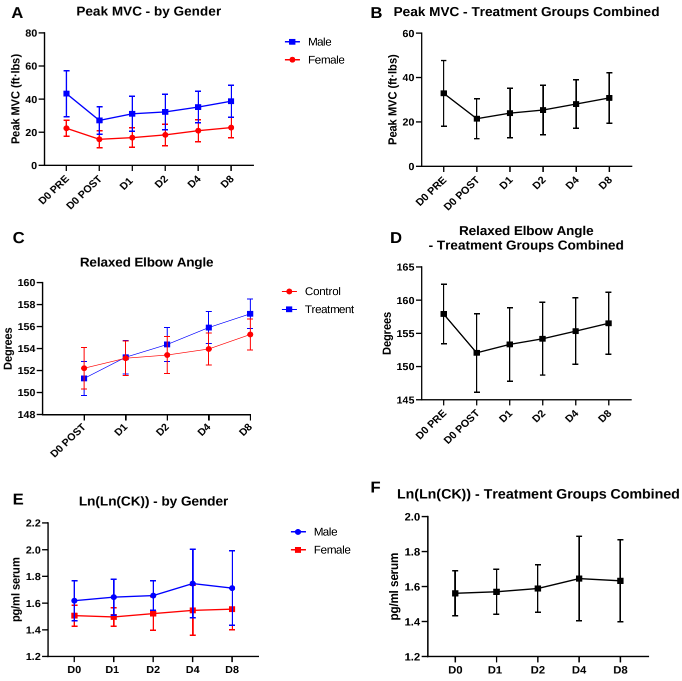

Figure 7. (A, B) Peak isometric MVCs (mean ± SD) over time. (C, D) Relaxed elbow angle (mean ± SD) over time. (E, F) Ln-Ln-transformed Creatine Kinase (CK) levels (mean ± SD) over time.

Treatment by Day interactions in this study suggest remedial effects of the CCAT regarding subjective outcomes (Figure 8), including ratings of arm pain and arm stiffness/soreness. Statistical trends were observed for subjective assessment of limitations in work and daily activities, and physical readiness. It is notable that for all of these subjective measures (shown in Figure 8), the responses of the Treatment group were consistently lower throughout the recovery period compared to the Control Group. It is generally observed that the rating peaked on 1 and 2 days post-exercise and recovered nearing Day 8. There were no adverse outcomes reported by the subjects due to the treatment.

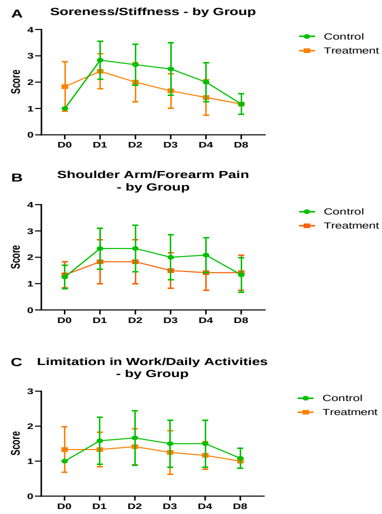

Figure 8. (A) Self-reported rating of soreness/stiffness of the DOMS arm (mean ± SD) over time. (B) Self-reported

rating of pain of the DOMS arm (mean ± SD). (C) Self-reported rating of limitations of work/daily activities (mean ± SD) over time.

All studies have inherent limitations and this one is certainly no different. Gender was observed to be a significant contributing factor of subjective outcomes of this study. The authors therefore suggest subjects with a variety of individual characteristics, such as gender, age and BMI, to be considered in the future and be recruited of sufficient sample sizes in order to gain understanding of the recovery and injury pathways of these sub-populations. While the sample size selected was similar to other studies of this sort, the sample size was somewhat small. This might have affected the ability to achieve significant results for certain measures. Furthermore, because subjects could not serve as their own control in this study (due to the conditioning effect obtained with eccentric exercise), differences between the treatment and control conditions were relatively large. However, this model of injury and repair of musculoskeletal tissues required such a design. Nonetheless, it is noteworthy that several significant differences existed in the pattern of responses for subjective and objective measures between control and treatment conditions. These findings contribute to improving the understanding of CCAT's effect on eccentric-exercise related DOMS.

In conclusion, Sigma Q® Bioneuro-based CCAT treatment resulted in a significant decrease in the self-reported ratings of the symptoms of pain, stiffness, and soreness post-eccentric-exercise. The treatment group demonstrated a significant rate of recovery post-exercise in relaxed elbow angle (REA), nearly twice that of the control group. Overall, treatment with the cumulative charge activation technology displayed substantial measurable improvement in flexibility and functionality recovery as well as considerable reduction in perception of pain post injury with no adverse effects on all measures of recovery.

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