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The Marc Pro™ Device Improves Muscle Performance and Recovery from Concentric and Eccentric Exercise Induced Muscle Fatigue in Humans: A Pilot Study

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ABSTRACT

Westcott WL, Chen T, Neric FB, DiNubile N, Bowirrat A, Madigan M, Downs BW, Giordano J, Morse S, LC Chen A, Bajaj A, Kerner M, Braverman E, Reini G, Blakemore M, Whitehead S, Sacks L, Blum K. The Marc Pro™ Device Improves Muscle Performance and Recovery from Concentric and Eccentric Exercise Induced Muscle Fatigue in Humans: A Pilot Study. **JEP^{online}** 2011;14(2):55-67. To date, a product or routine that consistently relieves delayed onset muscle soreness (DOMS) caused by eccentric exercise has yet to be identified. Our latest

research results indicate that a new device called Marc Pro™ (MPD) significantly improves muscle recovery and muscle endurance from combined concentric and eccentric exercise in healthy recreational exercisers. In the first study, 14 subjects (no prior soreness upon study entry) performed strength training activity (leg extension exercise with eccentric emphasis) to produce DOMS in the quadriceps muscles. All participants received one-hour of MPD stimulation on the right leg only following the exercise session whereby each participant served as their own control. One day later, assessment of muscle soreness revealed significantly less discomfort in the right leg (MPD) than in the left leg (no MPD) in all subjects and in responders, respectively ($p < 0.008$; $p < 0.002$). The number of repetitions completed with the right leg (MPD) was significantly greater than the number of repetitions completed with the left leg (no MPD) in all subjects and in responders, respectively ($p < 0.03$; $p < 0.008$). In the second experiment, 13 subjects (no prior soreness upon study entry) utilized a modestly challenging uphill/downhill hike to produce DOMS in the quadriceps muscles. Following the hike the subjects' right leg received MPD stimulation for 60 minutes, whereas the left leg received no MPD application. Reported soreness was significantly less in the right leg (MPD) than in the left leg (no MPD) in all participants and in responders, respectively ($p < 0.0008$; $p < 0.0002$). These results suggest that MPD stimulation results in a significant reduction in DOMS following strenuous unaccustomed eccentric exercise and significantly greater muscle endurance performance, as measured by leg extension repetitions. Investigation of Marc Pro™ in a larger population is underway and must await confirmation.

Key Words: Marc Pro™ Device (MPD), MARC, Muscle Recovery, Delayed Onset Muscle Soreness (DOMS), Concentric and Eccentric Exercise

INTRODUCTION

The Marc Pro™ Device (MPD) is a portable electronic muscle conditioning stimulator that uses a novel waveform and output parameters distinct from other available conditioning devices. It has received FDA clearance for muscle conditioning by stimulating muscle in order to improve or facilitate muscle performance. The MPD was designed to stimulate an ultra low frequency (1-2 Hz), low tension, non-tetanizing, and non-fatiguing contraction (32). Moreover, MPD technology has shown to produce a nitric oxide (NO)-dependent enhancement of microcirculation and angiogenesis in rats (32-33) and improve swim performance in athletes with concomitant reduction of plasma lactate (22).

We suggest that MPD causes enhanced performance and recovery due to conditioning of muscle through a number of powerful intracellular events in a cascade fashion that we have termed muscle activated recovery cascade (MARC™). The goal is to find a method to reduce delayed onset muscle soreness (DOMS) which has eluded most exercise physiologists. New information of muscle recovery physiology may provide clues into the mechanism of action (MOA) of MPD's beneficial effects on muscle recovery (2-9,11-16,18,24-30,34-35). These MOA involve new theories related to lactate; how NO levels stimulate mitochondrial biogenesis in muscle cells; and the involvement of the PPAR Gamma gene and production of co-activator (PGC)-1alpha as a potent transcriptional co-activator that regulates oxidative metabolism in a variety of tissues following exercise. Moreover, it has now been established that endurance exercise influences a number of cellular events including microcirculation to muscle tissue, production of NO, and angiogenesis which are all innate properties of MPD (32-33).

Delayed-onset muscle soreness (DOMS) due to Eccentric Exercise

While prolonged concentric or isometric muscle contractions lead to temporary fatigue, unaccustomed eccentric exercise results in prolonged fatigue and soreness well known as delayed onset muscle soreness or DOMS (3). In fact there are 204 PUBMED listed articles on DOMS

(9/17/10). Briefly, during a series of eccentric contractions, more and more sarcomeres are overstretched, beginning with the weakest and including progressively stronger sarcomeres. Each time the muscle relaxes, myofilaments in some overstretched sarcomeres may not reinterdigitate, and the sarcomeres lie scattered at random along the length of the myofibril. Moreover, when one or more sarcomeres have become disrupted, the damage may spread longitudinally to adjacent sarcomeres in the myofibril and transversely to adjacent myofibrils. These structural distortions produced by the presence of overstretched sarcomeres lead to membrane damage, including membranes of the sarcoplasmic reticulum, transverse tubules, or the sarcolemma. Finally, this is accompanied by the uncontrolled movement of calcium ions (Ca^{2+}) into the sarcoplasm, triggering soreness.

Once the damage process has reached the stage of ruptured membranes and there is a rise in resting intracellular Ca^{2+} , this resultant phenomenon induces proteolysis and facilitates breakdown of the damaged fibers. The accompanying inflammatory process involves invasion of damaged areas by macrophages and monocytes including histamine, serotonin, substance P, and prostaglandins that act to sensitize muscle nociceptors served by Gp111 and GpIV afferent fibers. The onset of inflammation roughly parallels that for soreness and could be present from 1-4 days depending on the severity of the eccentric exercise. The so-called soreness observed in DOMS is really tenderness. This sensation is experienced only during mechanical stimulation- contracting, stretching, or palpating the muscle. We therefore hypothesize that using MPD, which induces a rapid increase of microcirculation and fluid shifts, would ultimately lead to a reduction of DOMS. Additionally there is also evidence pointing to a central nervous system (CNS) mechanism involved in DOMS (22,31). It is conjectured herein that MPD stimulation may reduce DOMS by both peripheral NO mechanisms and systemically induced central mechanisms involving NO-induced microcirculatory properties.

The most current consensus attributes DOMS to microscopic tears in the muscle and surrounding connective tissue following eccentric exercise. A muscle contracts eccentrically when it lengthens under tension during exercise. Eccentric contractions also occur during aerobic activity, such as downhill running or walking, in which the quadriceps muscle repeatedly lengthens against gravity to lower the center of mass under control and aid in shock absorption. Moreover, Eston et al. (13) showed that muscle soreness following a downhill run, as expressed by the decrease in strength performance and the increase in plasma creatine kinase activity, were reduced when 100 maximal isokinetic eccentric quadriceps actions were performed 2 weeks before the event. While this may suggest a protective effect it does not address the common problem associated with DOMS from eccentric exercise. We therefore incorporated a downhill experiment in this study to determine the potential benefit of MPD following downhill eccentric exercise.

Finally the numbers of studies to identify the best methods to alleviate DOMS are almost as abundant as the number of studies conducted to determine its cause (10,36). These modalities include cryotherapy, massage, stretching, and the use of non-steroidal, anti-inflammatory drugs (NSAIDs), among other less conventional approaches. As of 2010, the literature presents no consensus on a consistent therapy to effectively reduce the soreness and fatiguing effects of DOMS.

Thus we elected to evaluate the role of the MPD in both simple eccentric resistance exercise as well as downhill walking exercise in humans. To our knowledge this is the first set of experiments to utilize this novel putative anti-nociceptive product to induce muscle recovery and enhance muscle endurance while concomitantly reducing DOMS.

METHODS

All stimulation was performed using the commercially available Marc Pro™ Device (Figure 1, Huntington Beach, CA), which has output parameters that are distinct from other available electronic muscle conditioning devices. For consistency it is to be noted that all MPD applications were

performed by one researcher and all other technical procedures were performed by another researcher knowledgeable about DOMS.



Figure1. Marc Pro™ Device

Experiment #1

To examine the effects of the MPD on muscle recovery (fatigue and soreness), our laboratory conducted two independent studies involving different activities for inducing eccentric action muscle micro-trauma and assessing muscle recovery as measured by reduction in muscle fatigue and soreness. All participants were surveyed to determine if they were healthy and soreness free at the beginning of the experiment. One-hundred percent (100%) were soreness free. In the first study (#1) the paradigm consisted of strength training activity (leg extension exercise) to produce micro-trauma in the quadriceps muscles. Each subject served as his/her own control.

Quadriceps Response to High Intensity Leg Extension Concentric/Eccentric Exercise

For the first experiment, our laboratory recruited fourteen subjects (10 females and 4 males); age range from 16-82; ethnicity: Caucasians (100%) [Table 1].

Table 1. Demographics

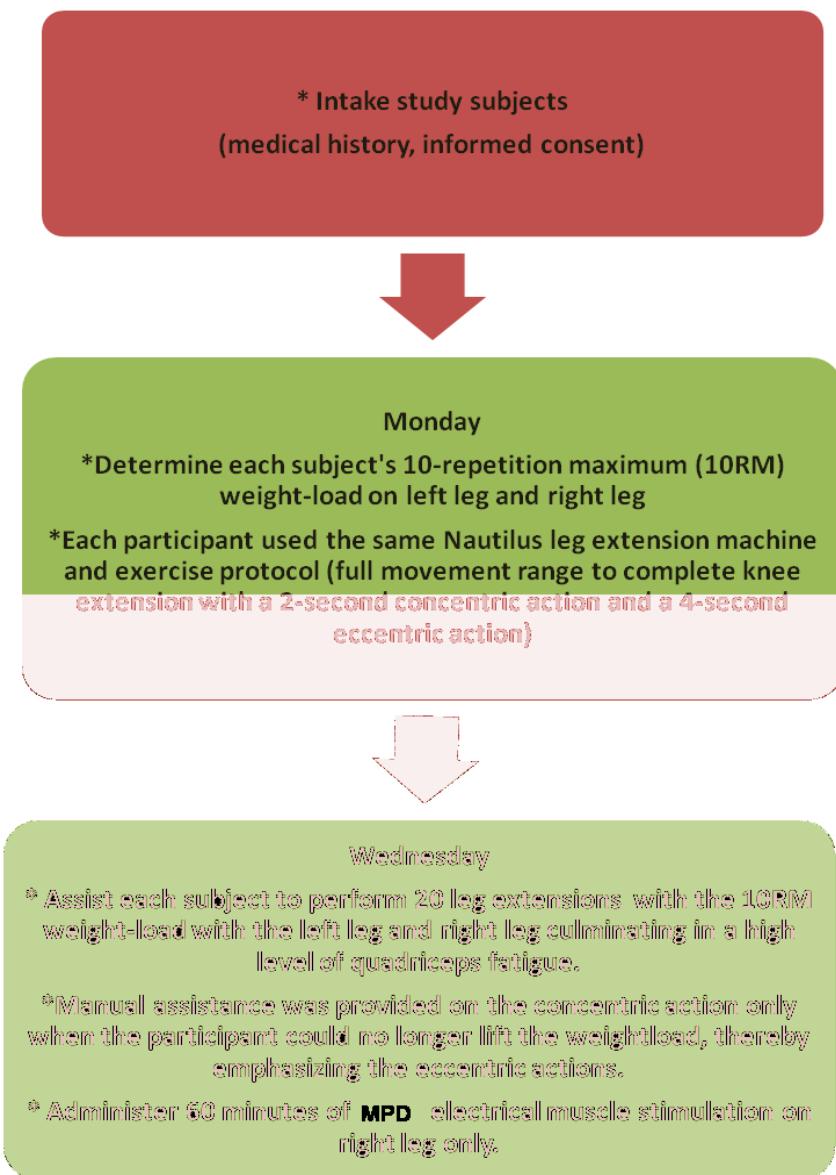
FACTOR	MALES	FEMALES	TOTAL
Sample size (n)	4	10	14
Age (yrs)	41.3 ± 26.4	45.1 ± 13.8	44.0 ± 18.4
Weight (lbs)	170.3 ± 41.2	167.0 ± 29.9	167.9 ± 33.6
Weight (kg)	77.4 ± 18.7	75.9 ± 13.6	76.3 ± 15.2

These subjects entered into the study meeting inclusion criteria and all subjects signed an informed consent statement. The PATH Research Foundation approved the research study (NIH registration # IRB00002334). This experiment featured a pilot study using MPD intervention to assess the effect on muscle recovery following a high-intensity bout of eccentric emphasis resistance exercise for the quadriceps muscles. For this study, knee extension repetitions were performed on a Nautilus® Leg Extension Weightstack machine Model 2ST (Nautilus, Inc., Fallbrook, CA).

The protocol is best exemplified in the flow chart presented in Figure 1. **Monday:** Each participant was assessed by successive trials using heavier weight-loads to determine the 10-repetition maximum resistance with the left leg and the right leg in performing knee extensions on the Nautilus 2ST leg extension machine. **Wednesday:** Each participant was trained beyond temporary concentric muscle fatigue with the left leg and the right leg by completing 20 repetitions with the previously established 10-repetition maximum resistance. When the subjects could no longer lift the weight-load,

appropriate manual resistance was provided by the investigators. Subjects lowered the weight-load without assistance, thereby emplacing eccentric muscle actions which are associated with greater DOMS than concentric (lifting) muscle actions. Immediately following these two exercise bouts (one for each leg), the right quadriceps received a 60-min MPD application (moderate intensity). The left quadriceps received no MPD. **Thursday:** Each participant was asked to rate the muscle discomfort in each quadriceps (left and right) on a 10-point scale with anchors of 1 (no discomfort) and 10 (extreme discomfort). Following this subjective evaluation, each subject performed as many repetitions as possible using the previously established 10-repetition maximum resistance with both the left leg and the right leg.

In this experiment each subject received a written and oral description of the study procedures. The subjects all received identical MPD stimulation administered by the same investigator, as well as the same time (10 min) after performing the supervised exercise. The follow-up interview and recording of the soreness rating with each subject was conducted in a private setting directed by the same investigator (WW) in order to reduce group interface and potential bias. Through a very carefully controlled stepwise procedure all start and stop times were recorded so that each subject received the MPD stimulation for exactly 60 min while sitting in an upright position.





Thursday

*Attain each subject's subjective rating of quadriceps discomfort (1-10 with 1 as lowest and 10 as highest) for the left leg and the right leg. Perform as many leg extensions as possible with the left leg and the right leg.

Figure 2. Schematic showing protocol for experiment #1.

Our laboratory conducted a second study using MPD intervention to assess the effect on quadriceps muscle recovery following a vigorous hike up and down Blue Hills Reservation of greater Boston. For the second study, 13 subjects (having no current soreness) were recruited (7 males and 6 females); age range from 30-56; ethnicity: Caucasians (100%) [Table 2].

Table 2. Demographics

FACTOR	MALES	FEMALES	TOTAL
Sample size (n)	7	6	13
Age (yrs)	45.7 ± 9.7	48.8 ± 10.8	46.8 ± 10.3
Weight (lbs)	184.4 ± 30.5	156.3 ± 9.6	174.2 ± 28.5
Weight (kg)	83.8 ± 13.9	71.0 ± 4.4	79.2 ± 12.9

The thirteen subjects participated in the experimental hike up and down the Blue Hills according to their own fitness levels and feelings of fatigue. All the subjects did one loop of the course, some performed two loops, and a few completed three loops up and down Big Blue, as necessary to attain quadriceps muscle fatigue. Each loop required between 15 and 20 minutes for completion, depending on the hiker's physical ability. The object was to induce quadriceps muscle DOMS in each subject.

Following the hike, all of the participants drove (approximately 10 min) to the South Shore YMCA where they received one hour of MPD application (moderate intensity) on the quadriceps muscles of their right leg. Their left leg received no MPD application. Immediately after MPD application was completed, each subject walked up and down two flights of stairs and reported the level of muscle discomfort in each quadriceps. The rating scale included 10 progressive discomfort descriptions (a modified Oswestry Scale specific to the hiking experience) with anchors of 1 (no discomfort) and 10 (extreme discomfort).

Data Analyses

Data were collected on 14 subjects in the first study and on 13 subjects in the second study. Statistical analyses were performed by means of SAS using paired t-test procedures. A minimum value of $p < 0.05$ was used to establish statistical significance. We did not carry out a Bonferroni correction since we felt that analysis did not evoke alpha errors.

RESULTS

Experiment #1

In this first experiment each participant was evaluated for both muscle soreness and muscle endurance. The subjects were classified as responders and non-responders. For reasons that are presently unclear, the responders reported relatively high levels of discomfort in both quadriceps

following the exercise session and prior to MPD intervention, but reduced soreness in their right quadriceps after the MPD application. The non-responders generally reported relatively low levels of discomfort in both quadriceps following the exercise session (level 2 or less on the 10 point scale).

Soreness and Fatigue Evaluation

On the average, the subjective rating for the left quadriceps (no MPD) was 3.3 ± 2.22 on the discomfort scale, whereas the subjective rating for the right quadriceps (MPD) was 1.5 ± 0.84 on the discomfort scale ($M = 1.7 \pm 2.1$, $t(13) = 3.11$, $P = 0.008$, 95% CI, 0.52 – 2.91).

When we evaluated the differences of MPD and no-MPD in terms of soreness , in only the responders ($n = 9/14$ or 64%), we found a more robust significant difference, whereas subjective rating for the left quadriceps (no-MPD) was 4.4 ± 1.86 on the discomfort scale compared to the right quadriceps (MPD) which was 1.7 ± 1.00 ($M = 2.8 \pm 1.80$, $t(8) = 4.62$, $p = 0.002$, 95% CI, 1.39 – 4.16) [Figure 3].

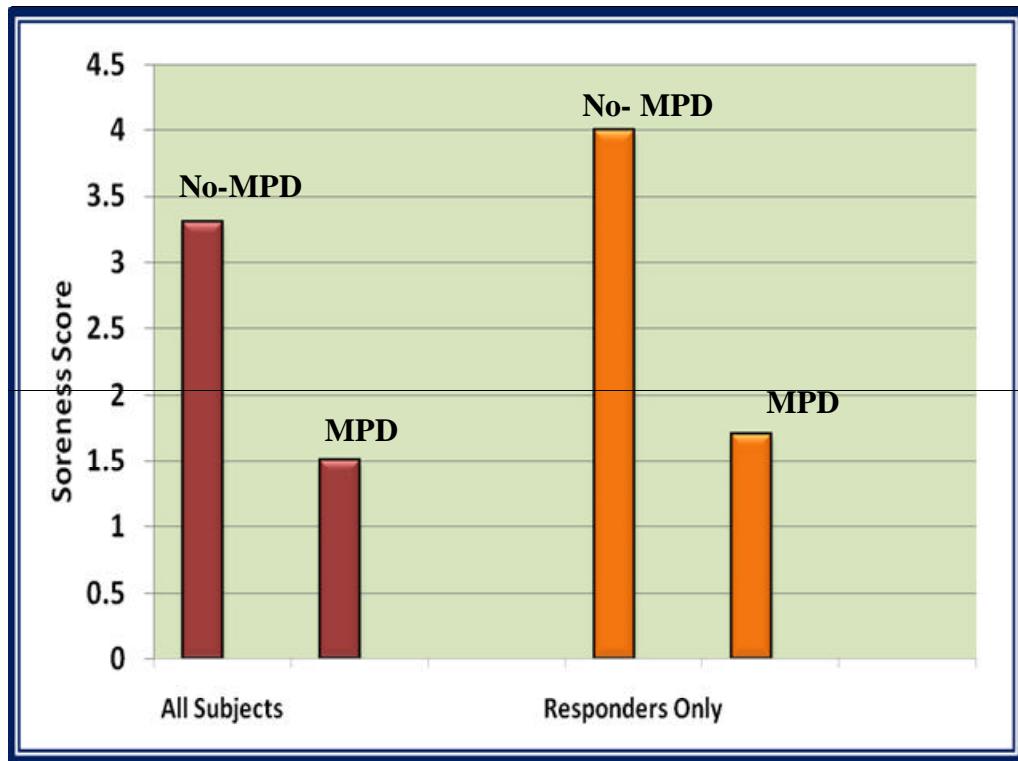


Figure 3. Illustrates the reduction of DOMS in all subjects ($n = 14$) and in responders only ($n = 9$). There was a significant difference between MPD and No MPD in all subjects tested ($p < 0.008$). Moreover there was even a greater significant difference ($p < 0.002$) between MPD and No MPD in the responders only.

Muscle Endurance

Muscle endurance was assessed in all 14 subjects by the number of repetitions completed with the original testing weightload. On the average, the number of repetitions completed with the left quadriceps (no MPD) was 14.6 ± 4.42 , whereas the number of repetitions completed with the right quadriceps (MPD) was 16.1 ± 4.34 ($M = 1.5 \pm 2.35$, $t(13) = 2.39$, $p = 0.033$ 95% CI = 0.15 – 2.85). Correspondingly, the responders ($n = 9$) completed 13.9 ± 3.69 repetitions with their left quadriceps (no MPD) compared to a 16.4 ± 3.81 repetitions with their right quadriceps (MPD) whereby P ($M = 2.5 \pm 2.19$, $t(8) = 3.51$, $p = 0.008$, 95% CI = 0.88 – 4.24) [See Figure 4].

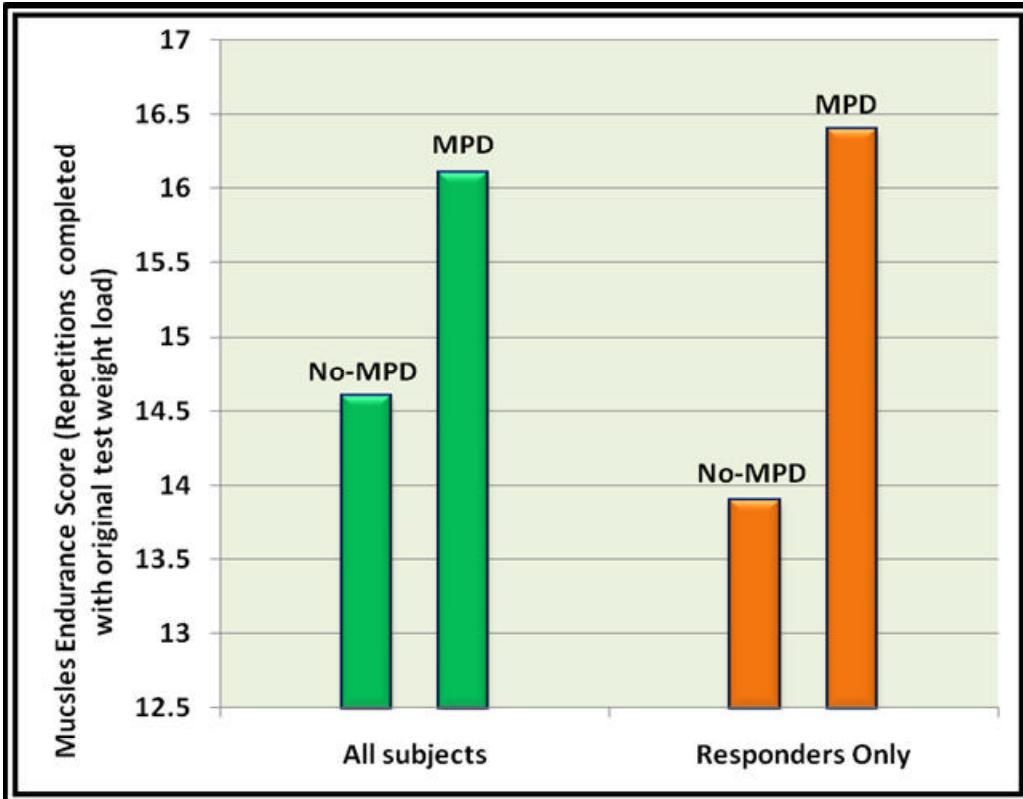


Figure 4. Illustrates the enhancement of muscle endurance performance as measured by number of leg extensions completed with the original testing weightload in all subjects ($n = 14$) and in responders only ($n = 9$). There was a significant difference between MPD and No MPD in all subjects tested ($p < 0.033$). Moreover there was even a greater significant difference ($p < 0.008$) between MPD and No MPD in the responders only.

Experiment #2

Soreness and Fatigue Evaluation

On average, the post-hike subjective rating for the left quadriceps (no MPD) was 3.7 ± 1.97 on the discomfort scale, whereas the subjective rating for the right quadriceps (MPD) was 1.7 ± 0.95 on the discomfort scale ($M = 2.0 \pm 1.63$, $t(12) = 4.42$, $p = 0.0008$, 95% CI = 1.01 – 2.99). Moreover, on average, the responders only (10/13 or 77%) had a 4.3 ± 1.83 discomfort level in their left quadriceps (no MPD) compared to a 1.7 ± 1.06 discomfort rating in their right quadriceps (MPD) following MPD application ($M = 2.6 \pm 1.35$, $t(9) = 6.09$, $p < 0.0002$, 95% CI = 1.6 – 3.6) [See Figure 5].

DISCUSSION

The findings of this study provide the first evidence that MPD stimulation significantly reduces DOMS caused by eccentric exercise. In the first phase of this study (experiment #1) the average subjective rating for the left quadriceps (no MPD) was 3.3 ± 2.22 on the discomfort scale, whereas the subjective rating for the right quadriceps (MPD) was 1.5 ± 0.84 on the discomfort scale ($p < 0.008$). This significant difference was further highlighted by the fact that among the responders (as defined herein) we found a more robust significant difference. Specifically, subjective rating for the left quadriceps (no MPD) was 4.4 ± 1.86 on the discomfort scale compared to the right quadriceps (MPD) was 1.7 ± 1.00 ($p < 0.002$).

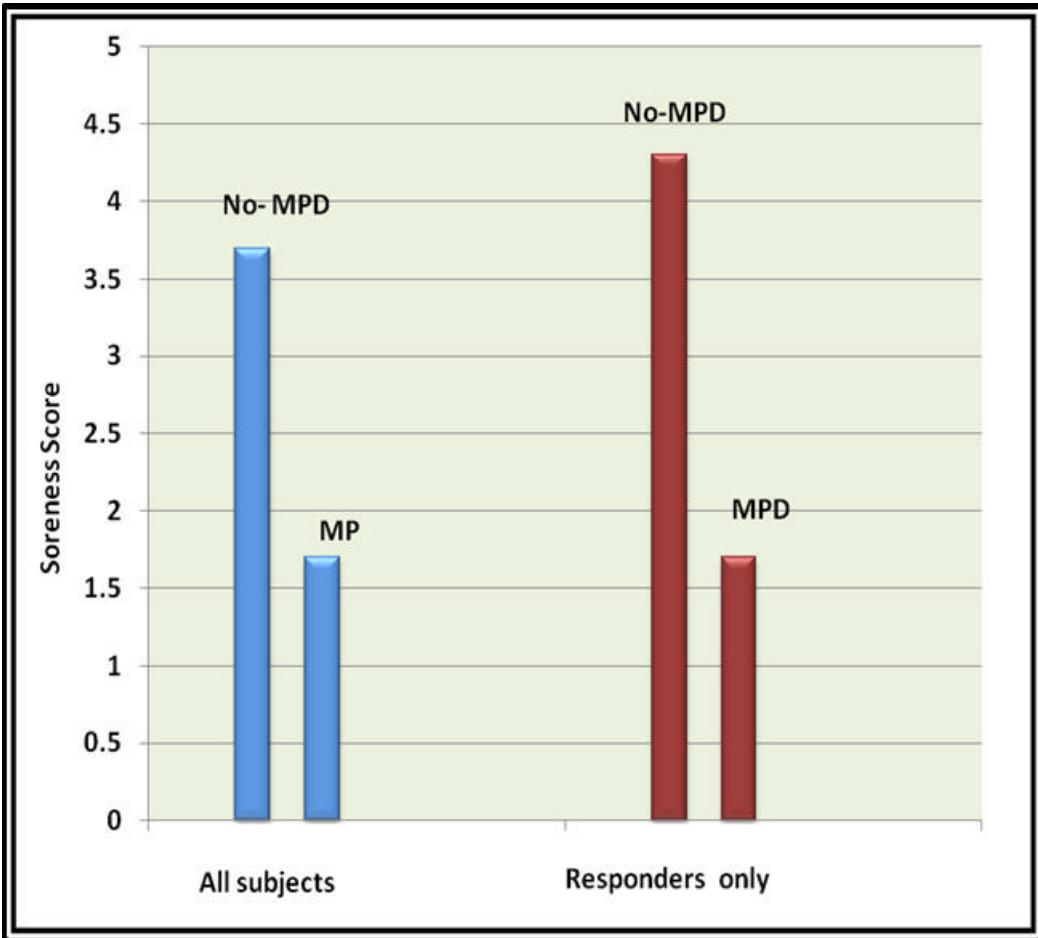


Figure 5. Illustrates the reduction of DOMS in all subjects ($n = 13$) and in responders only ($n = 10$) subjected to the Blue Hills hike. There was a significant difference between MPD and No MPD in all subjects tested ($p < 0.0008$). Moreover there was even a greater significant difference ($p < 0.0002$) between MPD and No MPD in the responders only.

Moreover, muscle endurance was assessed by the number of repetitions completed with the original testing weightload. As stated earlier, on average, the number of repetitions completed with the left quadriceps (no MPD) was 14.6 ± 4.42 , whereas the number of repetitions completed with the right quadriceps (MPD) was 16.1 ± 4.34 ($p < 0.033$). Correspondingly, the responders completed 13.9 ± 3.69 repetitions with their left quadriceps (no MPD) compared to a 16.4 ± 3.81 repetitions with their right quadriceps (MPD), whereby $p < 0.008$. Each leg served as its own control thereby eliminating any problem related to leg dominance.

We confirmed the effect of MPD on DOMS reduction by incorporating the second experiment involving eccentric emphasis aerobic exercise. On average, the post-hike subjective rating for the left quadriceps (no MPD) was 3.7 ± 1.97 on the discomfort scale, whereas the subjective rating for the right quadriceps (MPD) was 1.7 ± 0.95 on the discomfort scale ($p < 0.0008$). Moreover, on the average, the responders had a 4.3 ± 1.83 discomfort level in their left quadriceps (no MPD) compared to a 1.7 ± 1.06 discomfort rating in their right quadriceps (MPD) one hour after MPD application ($p < 0.0002$).

While the mechanism of increased muscle recovery from eccentric exercise due to MPD is unknown, it is possible that this finding may be due to MPD's putative cellular responses (i.e., NO production, fluid shifts, protein clearance, angiogenesis etc), as well as its potential to induce mRNA transcriptional proteins such as PPAR gamma co-activator (PGC)-1alpha, and VEGF (2,11,21,32-33).

However since we did not perform any biochemical analysis pre-and post-MPD the mechanism remains unknown. The mechanism of action (MOA) must await future perspective research in larger populations.

While there is a limitation to the interpretation of these findings due to the relatively small sample size, we are encouraged by the significant P values obtained. We are cognizant that a few outliers may reduce the significant findings. However, these positive findings are a reflection of the both scientific rigor in the execution and strict adherence to established protocol. Another important caveat may have to do with the characteristics of the subjects in the current study. We may have different results in people who are not healthy recreational exercisers, and certain physiological characteristics may impact the positive MPD outcomes. These include but are not limited to: weight; BMI, percent body fat; height, gender; age; ethnicity, and genetic polymorphisms and gene expression. In our recently completed (unpublished) strength training study with 80 adult participants, the 43 subjects who performed post-exercise electrical muscle stimulation (Marc Pro™ Device) experienced significant ($p < .01$) reductions in their ratings of low-back fatigue, thereby supporting the findings in this study.

CONCLUSIONS

All forms of exercise, if carried out vigorously enough, can cause muscle fatigue and/or temporary self-limiting soreness. But only one form of very specific muscle training, eccentric exercise, will predictably produce a very specific type of muscle soreness the next day and up to 3-4 days. To date, a product or routine that consistently relieves delayed onset muscle soreness (DOMS) has yet to be identified. The current study provides follow-up to the investigation by Neric et al. (22) that demonstrated reduction of plasma lactate levels following MPD technology in sprint swimmers with concomitant muscle recovery.

The studies presented in this paper indicate that MPD may significantly improve muscle recovery and muscle endurance from combined concentric and eccentric exercise involving healthy recreational exercisers. We propose that the reduction of DOMS may be due to both known and suspected innate properties of MPD stimulation consisting of complex cellular responses generating a cascade of recovery events we term “muscle activated recovery cascade” (MARC™). The importance of electromyostimulation (EMS) as an alternative method to enhance health benefits especially in the elderly is amplified by the recent work of others. Kemmler et al. (20) found that EMS training significantly exceeds the effect of isolated endurance and resistance type exercise on fitness and fatness parameters. They conclude that for elderly subjects unable or unwilling to perform dynamic strength exercises, EMS [e.g., MPD] may be an alternative to maintain lean body mass, strength, and power.

Due to the small sample size, this research warrants extensive further investigation in larger samples, selective identifiable candidates, genetic expression and further measurement of neurohumeral, mitochondrial biogenesis kinetics of cellular lactate absorption following MPD application under both concentric and eccentric exercise paradigms (1,4-6,7,11,15-17,19,20,25). We are confident, because of known properties of MPD technology derived from animal studies showing NO-dependent enhanced microcirculation, muscle loading and angiogenesis; the improved muscle recovery and performance from concentric and eccentric exercise induced muscle fatigue in humans, demonstrated in this paper will be confirmed in larger studies. We cautiously await further confirmation in a larger population.

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Conflict of Interest

Kenneth Blum, Nicholas DiNubile, Gary Reinl, and Lester Sacks are paid consultants for Marc Pro™, Huntington Beach, California. All other authors do not disclose any conflict of interest.

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