The microvascular and hemodynamic mechanisms for the therapeutic actions of H-Wave® muscle stimulation

Thomas L. Smith[1], Kenneth Blum[2,3], Roger Waite[3], W.J. Jim Heaney[3], Michael Callahan[1,2]
[1]Orthopaedic Surgery, Wake Forest University School of Medicine, Winston-Salem, NC; [2]Physiology and Pharmacology, Wake Forest University School of Medicine, Winston-Salem, NC; [3]Electronic Waveform Lab, Inc, Huntington Beach, CA

Introduction: H-Wave® is a therapeutic electrical stimulation modality demonstrated to reduce swelling and relieve pain following soft tissue injury. The mechanism of action of this modality is unclear, but may be related to improving perfusion to the affected tissue, with the potential for reducing the extravasation of fluid and minimizing edema. The aim of the current study was to directly assess striated muscle microvascular responses to H-Wave® stimulation (HWS). In addition, the effect of repeated stimulation over a three week period on hindlimb blood flow was assessed. It was hypothesized that acute electrical stimulation of striated muscle would result in arteriolar vasodilation, and that repeated therapeutic electrical stimulation would result in an increased perfusion capacity in the treated muscle.

Materials and Methods: ***Microvascular***- The microvasculature of 57 male, S-D rats was studied using compound intravital microscopy and electrical stimulation. Rats were anesthetized with urethane (1g/kg, i.p.), and the left cremaster muscle prepared for videomicroscopy using a modification of the Baez technique[1]. Platinum electrodes were used for electrical stimulation of the tissue. One arteriole per rat was measured before, during, and after electrical stimulation of the cremaster muscle for up to 2.5 hours. The cremaster muscle was stimulated at either 1 Hz or 2 Hz for periods of 30-60 min. Control rats (n=15) were not exposed to electrical stimulation during the intravital microscopic evaluations. The role of nitric oxide (NO) in the microvascular response to HWS was assessed by blocking the NO pathway using L-NAME, topically applied at 10^{-5} M to the cremaster prior to electrical stimulation at 2Hz (n=10 rats). Maximal arteriolar responses to H-wave stimulation were measured and compared to pre-stimulation diameters. Student's t-test for paired data was used to determine significant differences before and during stimulation. ***Blood Flow*** – Limb blood flow was studied in 10 male, S-D rats. Animals were assigned to a stimulation-conditioned group ("Conditioned") or a sham stimulation group ("Sham")(n=5/group). The Conditioned group was treated with 1 hr of 2 Hz electrical stimulation to the left leg daily (M-F) for three weeks. The "Sham" group was treated with anesthesia only for an equivalent period. The contralateral limb in both groups served as the control limb. After 3 weeks, rats were anesthetized with isoflurane, and iliac artery blood flow was measured bilaterally using ultrasound transit-time flowmetry before, during, and after acute HWS of each hindlimb for 5 minutes. Differences between Conditioned or Sham hindlimb blood flows, compared to the control side, were analyzed using Student's t-test for paired data.

Results: ***Microvascular*** - HWS both at 1 and 2 Hz resulted in significant arteriolar vasodilation (Fig. 1). The arterioles in control animals, not exposed to electrical stimulation, demonstrated no changes in diameter. Microvascular diameters did not change with HWS following blockade of NO (84.1 ± 4.5 μm pre- v. 84.7 ± 4.1 μm post-stimulation).

The control leg increased blood flow by 200 percent. Sham animals did not demonstrate a between-leg difference (Sham leg v. control leg).

Discussion: Significant arteriolar dilation induced by HWS suggests that this treatment modality is associated with significant increases in striated muscle perfusion. Because of Poiseuille's Law, the observed increases in arteriolar diameter translate into increases in blood flow of 26-62%. Therefore, HWS of striated muscle using clinical stimulation parameters results in a physiologic response characterized by microvascular arteriolar dilation. In addition, arteriolar dilation is not observed following HWS in the presence of L-NAME blockade of NO production, suggesting that the microvascular response to HWS is mediated, at least in part, by NO.

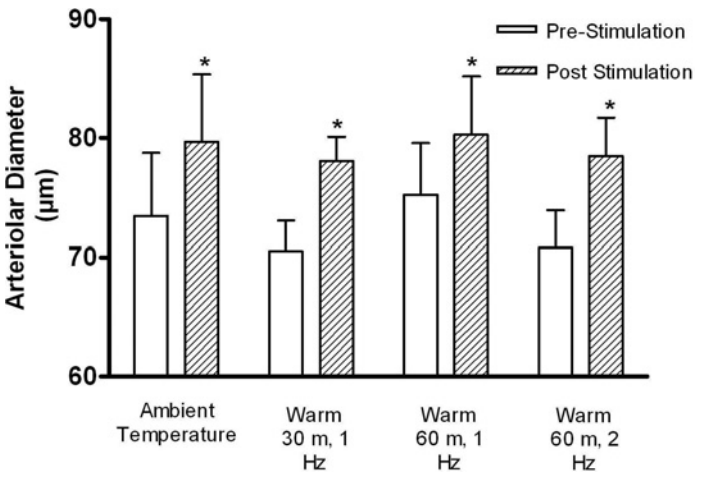

Figure 1. Microvascular diameters before and after electrical stimulation for 30 or 60 min at 1 or 2 Hz stimulation. * p<0.05 pre v. post

Blood flow - HWS of the Conditioned hindlimb elicited an average 247 percent increase in limb blood flow above resting conditions.

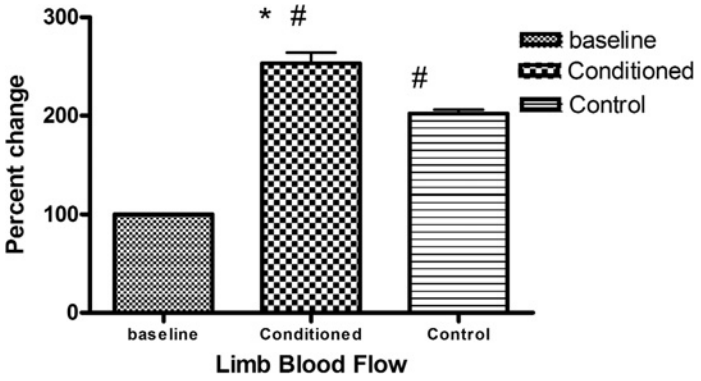

Figure 2. Limb blood flow in HWS Conditioned versus control limbs during electrical stimulation, compared to pre-stimulation baseline values (* P< 0.05) ; # p<0.05 compared to baseline. N=5 rats.

Limb blood flow changes accompanying HWS corroborated the microvascular findings, demonstrating a significant increase in limb blood flow accompanying HWS. In addition, repetitive daily exposure to HWS for 3 weeks elicited a 25% greater increase in blood flow in the HWS conditioned limb compared to the contralateral non-conditioned control limb. This increase in blood flow in the Conditioned limb suggests an increased vascular reserve available for augmenting perfusion in the limbs exposed to repetitive HWS.

These microvascular and hemodynamic findings provide an understanding of the mechanisms associated with increased perfusion accompanying therapeutic electrical stimulation of skeletal muscle using the HWS frequency and waveform.

References: 1. SmithTL, Wong-Gibbons D, Maultsby J. Microcirculatory effects of pulsed electromagnetic fields. JOR 2004; 22:80-84.

Acknowledgements: Supported, in part, by Electronic Waveform Lab, Inc. and the Musculoskeletal Research Center of the Wake Forest University School of Medicine.