

Electrically Stimulated Eccentric Contraction Training for Composite Trauma Recovery

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INTRODUCTION: Orthopedic trauma typically involves volumetric muscle loss (VML), defined as the surgical or traumatic loss of muscle tissue (>20%), resulting in functional impairment. Although VML injuries are typically studied in isolation in preclinical research, they frequently occur alongside bone fractures in orthopedic trauma cases [1]. Clinically, the focus is on fracture repair, with multiple FDA-approved treatments available. To maximize functional recovery, a rigorous physical therapy regimen is often implemented following composite orthopedic injuries. Our lab had previously developed an electrical stimulation-based eccentric contraction training (ECT) protocol for VML-injured animals, which increased muscle mass, function, and myofiber size [2]. In this work, the ECT protocol was implemented in a rat model of muscle-bone trauma combining VML and a segmental bone defect (SBD), where we aim to determine the effects of ECT on both muscle and bone recovery. We hypothesized that animals that received ECT would exhibit improvements in fracture bridging, muscle torque production, and muscle mass compared to animals that did not receive ECT.

METHODS: All animal procedures were approved by Saint Louis University's IACUC (protocol #2645). Male Lewis rats (aged 2-3 months) received VML and SBD injuries. SBD was created by removing a 2-4 mm segment of the tibia, followed by internal fixation with a PEEK plate and screws. VML injury was created by removing ~20% of the muscle mass from the adjacent tibialis anterior (TA) muscle with a 6 mm biopsy punch. The right contralateral leg was left uninjured. After 21 days of recovery post-injury, animals underwent either ECT (n=3) or no ECT (n=3) for four weeks. Rats were placed on a heated platform, with their left foot secured to a foot pedal and two electrodes inserted subcutaneously onto the peroneal branch of the sciatic nerve to ensure that only the muscles of the anterior compartment were activated. Passive (or unstimulated) range of motion stretching was initiated for three repetitions before beginning ECT. In every ECT session, four sets of five eccentric contractions were performed with simultaneous stimulation of the peroneal nerve at 150 Hz, separated by two minutes of rest between sets. Animals receive two ECT sessions per week, with 2-3 days of rest in between. Eccentric torque values were recorded at the beginning of each set and averaged for each session. At the terminal time point (day 49 post-injury), peak isometric torque was measured at 150 Hz before euthanasia and collection of blood, muscle, and bone tissues.

RESULTS: After 4 weeks (or eight sessions) of ECT, the increase in average eccentric torque between the first and the last session was determined to be 14.18 N-mm, suggesting an overall progressive improvement in strength. The peak isometric torque (normalized to body weight) was statistically higher, showing a ~37% improvement in the ECT group relative to the non-ECT group (One-way ANOVA, p=0.0014). These results potentially indicate myofiber hypertrophy and increased recovery from composite trauma, which will be investigated histologically in future studies. TA muscle mass showed significant differences between uninjured contralateral controls and injured groups (1-way ANOVA, p<0.0001), with ~19% improvement in the ECT group relative to the non-ECT groups when normalized to body weight (1-way ANOVA, p=0.0247). All fractured bones were found to be partially bridged by the terminal time point (day 49). The impact of ECT on fracture bridging will be assessed in future studies.

DISCUSSION: These results suggest that even with an adjacent segmental bone fracture, the VML-injured muscle remains responsive to mechanical loading and can positively adapt to eccentric exercise. In our previous study, ECT was implemented 14 days post-VML injury to allow for the inflammation to subside and for the muscle to recover from the initial trauma to some extent. Due to the composite nature of the injury involving a bone fracture in combination with VML, we increased the recovery period to 21 days to prevent the displacement of screws and plates used for the internal fixation of the fractured tibia. However, the extent of functional recovery was found to be similar between the ECT and non-ECT groups in both studies (~37% improvement in peak isometric torque). Ongoing studies are focused on micro-CT and histological analysis of tibias, as well as histological and biochemical analysis of injured muscle. To achieve sufficient power, more animals will be added to each experimental group in the coming weeks. A female cohort of age-matched animals will be added in future studies.

CLINICAL RELEVANCE: VML is a chronic injury that frequently occurs in cases of composite orthopedic trauma, leading to significant loss of muscle mass and impaired functional capacity. While physical therapy is the current standard of care, clinical subjects often reach a functional plateau beyond which no further gains are possible. In this work, we implemented ECT as a therapeutic strategy in a clinically relevant model of composite trauma involving tibia fracture in combination with adjacent VML injury. ECT or strength training has led to improvements in muscle strength in both rodents and humans in various other models of muscle injury and disease. However, ECT is understudied in the context of VML.

REFERENCES:

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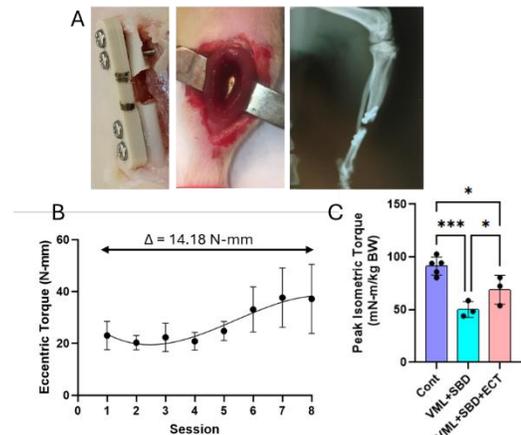


Figure 1. (A) Photographs depicting the surgical creation of the tibia fracture (left), and the VML injury (middle). X-ray shows unbridged fracture at 4 weeks post-injury (right). (B) Progressive increase in eccentric torque was observed between sessions 1 to 8. (C) Peak isometric torque showed a significant recovery with ECT application.