

# Can Intraoperative Electrical Nerve Stimulation Be Used to Predict Functional Recovery Following Median Nerve Stretch Injury in Rats?

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## INTRODUCTION:

Peripheral nerve injury commonly results in pain and long-term disability for patients. Recovery after incontinuity stretch or crush injury remains inherently unpredictable. Our inability to accurately distinguish injuries that will recover naturally from those requiring immediate surgical intervention makes surgical decision-making highly challenging and often results in delayed surgery with unsatisfying outcomes. A prognostic tool with the ability to distinguish different degrees of nerve injury and to predict recovery in the acute clinical setting is thus desperately needed. We therefore asked: (1) Can intraoperative electrical stimulation be used to distinguish two distinct degrees of acute stretch injury in the rat median nerve? (2) Can intraoperative stimulation be used to predict functional recovery following stretch injury in the rat median nerve?

## METHODS:

To answer our first research question, we enrolled twenty-two 12-month-old male Sprague-Dawley rats in a sham control (6 rats), an epineuroclasis (8 rats) and an endoneuroclasis (8 rats) group. Epi- and endoneuroclasis describe the first and second degree of mechanical and structural failure during stretching in the rat median nerve and serve as the first and second (more severe) stretch injury level in this study. The median nerves of both forelimbs were surgically exposed and probed with a handheld electrical stimulator to identify the stimulation threshold required to induce digit flexion. In both injury groups, nerves were then stretched to their respective injury levels using a hook attached to a load-cell that generated the load-deformation curve of the nerve in real-time. Nerves were secured under two metal pins and stretched until a first (epineuroclasis) or second (endoneuroclasis) sudden force reduction was observed on load-deformation curves. After the injury, rats in both injury groups were again probed with the stimulator to identify differences in stimulation thresholds between injury levels.

To answer our second research question about the ability to predict recovery after stretch injury in the rat median nerve, the grip strength of all rats was assessed using the grasping test at one week preoperatively, as well as at one, three, six, nine and twelve weeks postoperatively. Twelve weeks served as the final follow-up, after which rats were euthanized.

## RESULTS:

Intraoperative electrical stimulation allowed for differentiation of both injury levels based on the nerve's overall responsiveness to stimulation. Both injury levels required similarly high stimulation thresholds to induce digit flexion after stretch injury with 200 Nanocoulomb (nC) (range 100 to 1600 nC) after epineuroclasis and 200 nC (100 to 400 nC) after endoneuroclasis (difference: 0 nC,  $p = 0.74$ ). However, 15/16 nerves induced digit movement after epineuroclasis while only 5/16 nerves in the endoneuroclasis group induced a response at any stimulation threshold (OR = 33, [95% CI: 3.91 - 373.0],  $p < 0.001$ ). Lack of responsiveness at time zero was strongly associated with a lack of functional recovery. Both injury levels exhibited an acute loss of grip strength one week after injury. However, at twelve weeks, sham control and epineuroclasis rats demonstrated a similar grip strength with  $12.97 \pm 2.88$  Newton (N) and  $13.18 \pm 2.59$  N, respectively (difference -0.21 N, [95% CI -3.85 to 3.43 N],  $p = 0.99$ ). Endoneuroclasis resulted in a chronic loss of function compared to control rats with  $2.51 \pm 1.1$  N at twelve weeks (difference 10.45 N, [95% CI 6.81 to 14.1 N],  $p < 0.001$ ). Nerves that were unresponsive to stimulation had a 92% likelihood of no functional recovery (negative predictive value 0.92 [95% CI 0.64 to 1]). Conversely, nerves that responded to stimulation had a 75% probability of recovery (positive predictive value 0.75 [95% CI 0.53 to 0.89]).

## DISCUSSION AND CONCLUSION:

Two distinct degrees of acute stretch injury in the rat median nerve can be distinguished based on the ability to induce digit movement using a handheld electrical stimulator. In the rat median nerve, responsiveness to stimulation is predictive of long-term recovery after stretch injury and vice versa.

The ability to predict recovery using intraoperative nerve stimulation could allow surgeons to distinguish injuries that will likely recover naturally from those requiring immediate surgical intervention. A prognostic tool that correctly indicates nerve surgery in the acute clinical setting could facilitate more accurate surgical decision-making and drastically improve patient outcomes.

