

Calcium and Calcium-ATPase Levels During Peripheral Nerve Regeneration

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Objectives

Peripheral nerve injury can have devastating effects on daily life. The increase in calcium concentration after nerve injury can negatively impact neurite growth and activate downstream processes leading to neuron death.¹⁻³ Our previous studies have shown that calcium-modulating agents can decrease calcium accumulation in peripheral nerve tissues and improve the speed of functional recovery,⁴ however the effective therapeutic window has not yet been identified.

Methods

Twenty-four 3-month-old Sprague-Dawley rats were divided into 4 groups with different end-points: 2, 8, 12, and 24 wks. The left side served as the sham control while the right side sustained sciatic nerve crush injury. Measurements at each time point included compound muscle action potential (CMAP) from the extensor digitorum longus muscle, nerve calcium staining, and Ca²⁺-ATPase mRNA expression by qPCR.

Left

1. Open incision
2. Isolate sciatic nerve
3. Close incision

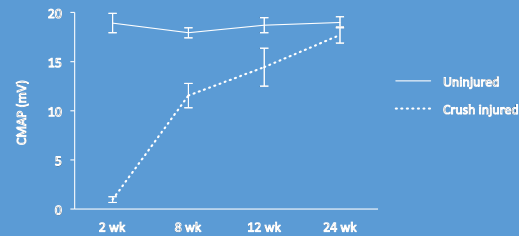


Right

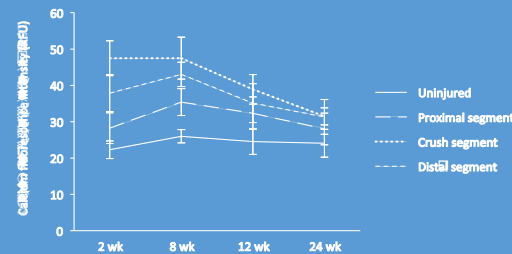
1. Open incision
2. Isolate sciatic nerve
3. Crush nerve
4. Close incision

Results

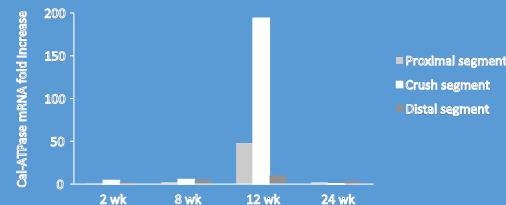
Functional recovery over time



Calcium levels over time



Calcium-ATPase levels over time



Discussion

We showed that after rat sciatic nerve injury, calcium accumulation remained at peak elevation past 8 wks before decreasing over 24 wks back toward baseline. At the same time, CMAP recovered to near normal.

Unexpectedly, qPCR results showed that upregulation of sarco/endoplasmic reticulum calcium-ATPase (SERCA; pumps cytosolic calcium into intracellular stores found in neurons and Schwann cells) mRNA remained only minimally elevated until 12 weeks when a near 200 fold increase was observed in the crushed nerve segment followed by return to baseline by 24 weeks.

These results taken together suggest that up-regulation of SERCA may account for the decrease in calcium accumulation, however the reason for the peak at 12 weeks will require further investigation.

These results may also imply that in order to achieve maximal benefit after peripheral nerve injury, therapies to decrease calcium accumulation should likely be initiated as soon as possible but may still be beneficial if started before the natural course of calcium decline which occurs after 8 weeks.

References

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