

Optimizing Nicorandil for Spinal Cord Protection in a Murine Model of Complex Aortic Intervention

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INTRODUCTION

- There are currently no pharmacological agents utilized to increase metabolic tolerance to spinal cord ischemia-reperfusion injury in the setting of complex aortic surgery.
- Nicorandil, a ATP-sensitive potassium (KATP) channel opener, has shown promise in neuroprotection.
- We hypothesized that 3 days of Nicorandil pretreatment confers effective neuroprotection via activation of the mitochondrial KATP channel.*

MATERIALS AND METHODS

- Spinal cord injury was induced by 7 minutes of thoracic aortic cross clamping in adult male C57BL/6 mice.
- Limb motor function was evaluated, viable anterior horn neurons quantified.

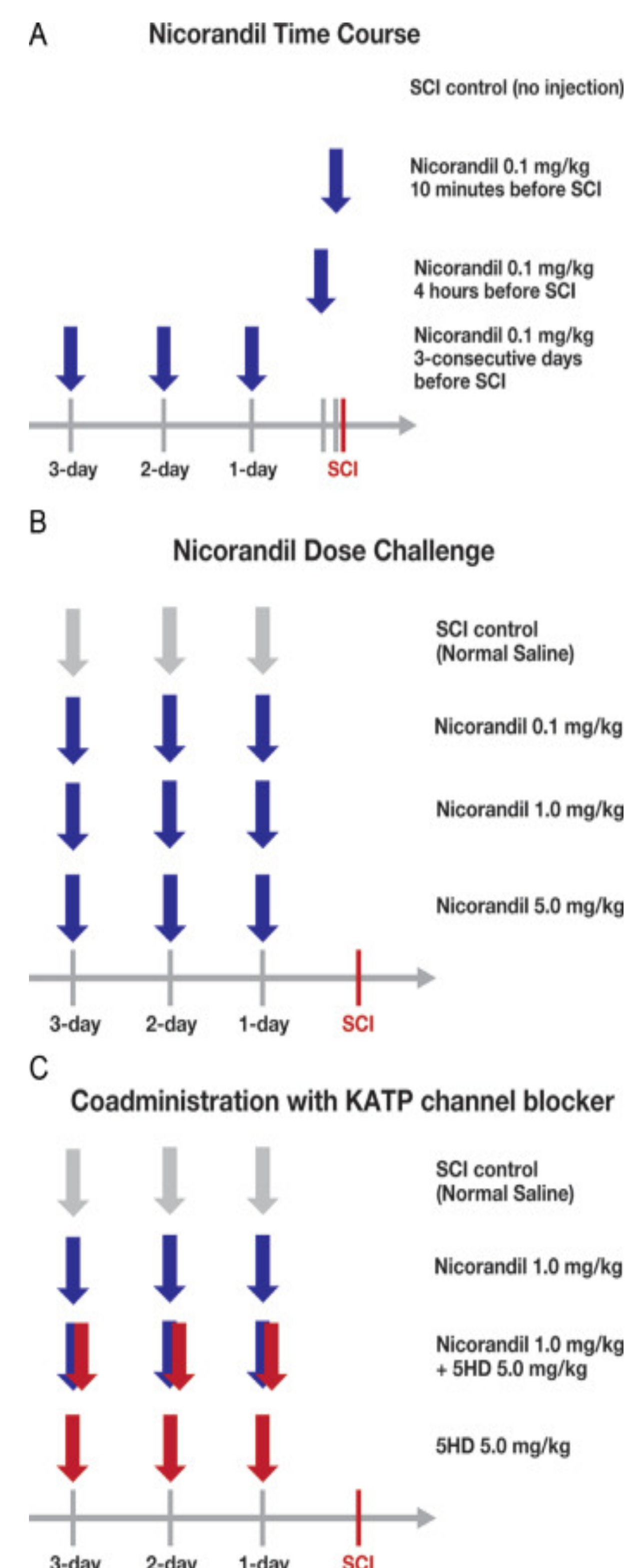


Figure 1: Experimental design for each group. (A) Nicorandil time course. (B) Nicorandil dose challenge. (C) Coadministration with KATP channel blocker.

RESULTS

- Nicorandil pretreatment at 4 hours and 3 days before ischemia significantly preserved motor function preservation.
- All Nicorandil doses showed significant motor function preservation.
- Neuroprotection was abolished by 5HD co-administration.
- Histological analysis showed significant neuron preservation with Nicorandil pretreatment, quantified with NeuN staining.

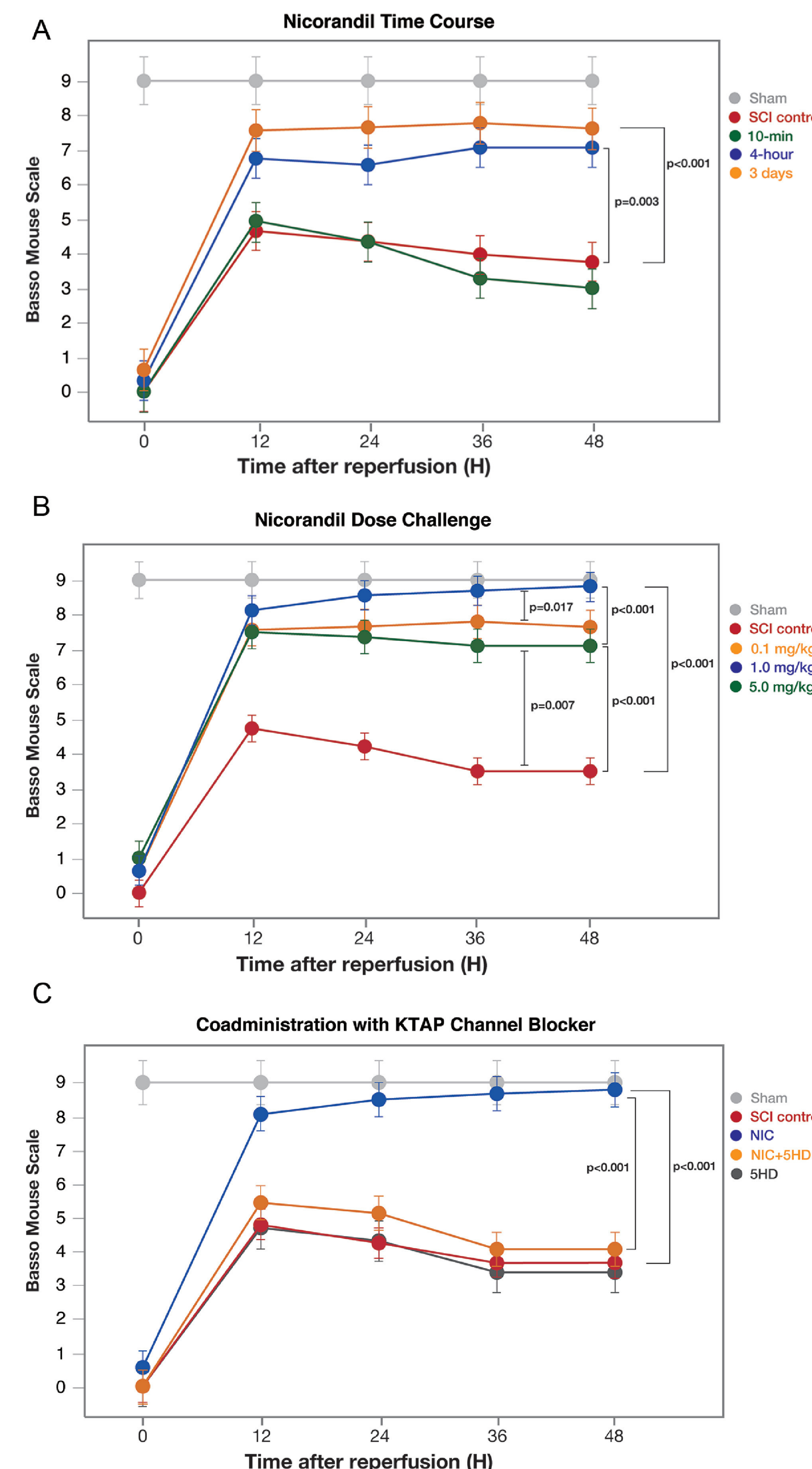


Figure 2: Mouse limb motor function after ischemia-reperfusion injury for each group is expressed as least square mean \pm standard error. .

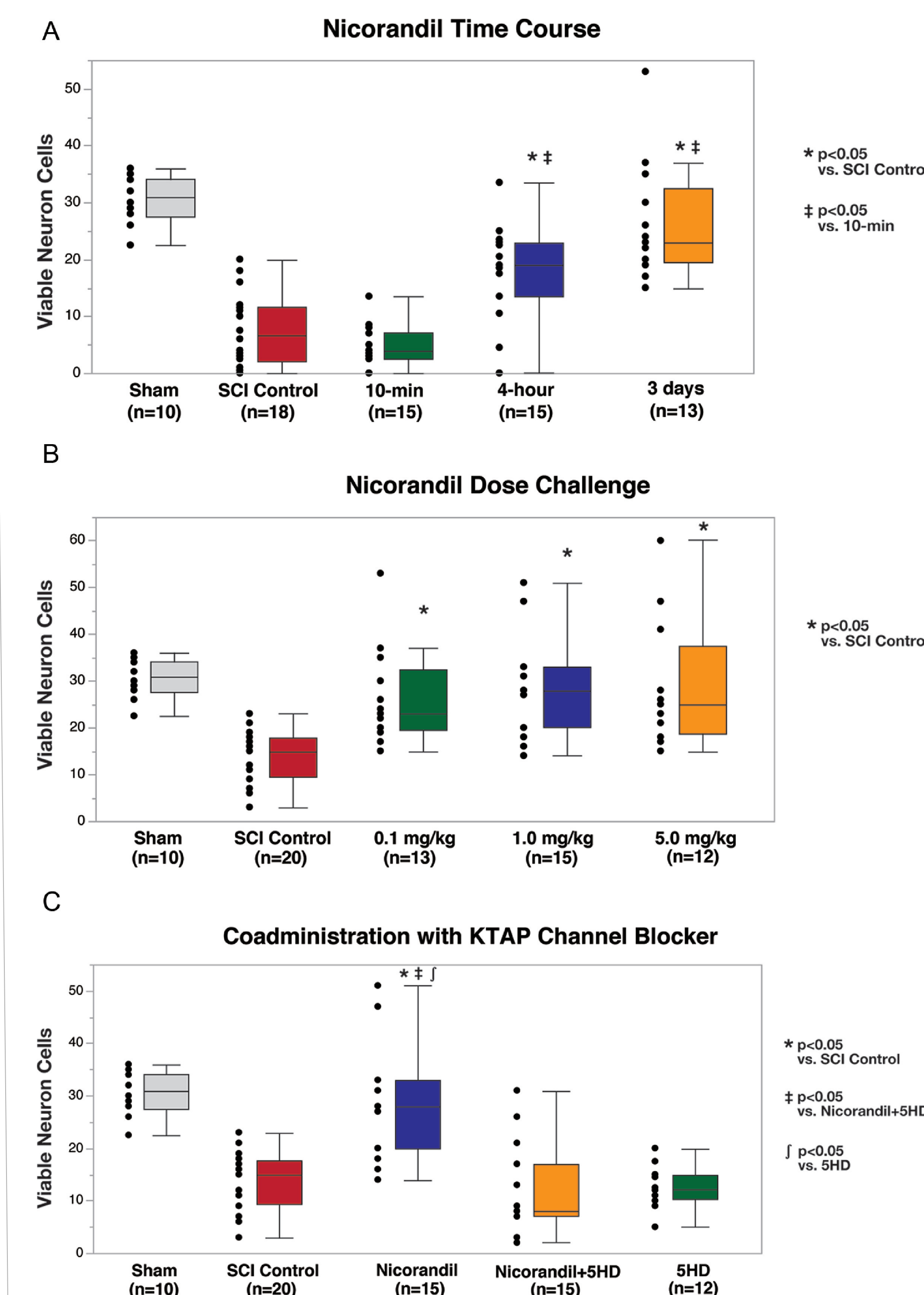


Figure 3: Number of viable neurons within a standardized section of the anterior horn of the spinal cord for each group using NeuN staining (10x magnification).

CONCLUSIONS

- Three days administration of Nicorandil 1.0 mg/kg showed near-total motor function preservation in a murine spinal cord ischemia-reperfusion model, mediated by the mitochondrial KATP channel.
- Further elucidation of the Nicorandil effect through KATP pathway is needed, unclear if acts through direct or indirect pathways.
- Nicorandil is a promising clinical and pharmacologic agent that may improve patient outcomes in the setting of complex aortic surgery.

Acknowledgements & Disclosures

Conflicts of Interest: None declared

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