



LONGITUDINAL NERVE AND MUSCLE CHANGES IN A MURINE MODEL OF CHRONIC NERVE COMPRESSION

Jagmeet S. Arora, BS; Allen Green, BS; Jordan J. Burgess, BA; Shannon D. Francis, MSc; Amar Singh, PhD; Paige M. Fox, MD, PhD
Division of Plastic and Reconstructive Surgery, Stanford University, Palo Alto, California, USA



Introduction

- Chronic peripheral nerve compression (CNC) has the potential to cause substantial morbidity with severity often depending on the duration of compression.
- Previous murine models have examined CNC for short durations.
- In this study, we characterize longitudinal nerve, muscle, and genetic changes over 52 weeks of nerve compression in a murine model.

Methods

- Three groups of increasing compression duration:
 - 16 weeks
 - 32 weeks
 - 52 weeks
- To induce compression, a silastic tube was placed around the left sciatic nerve with the contralateral nerve as a paired control.
- After compression, the following was collected and analyzed:
 - Electrodiagnostic data
 - Tibialis anterior and Gastrocnemius muscles
 - Sciatic nerves

Results

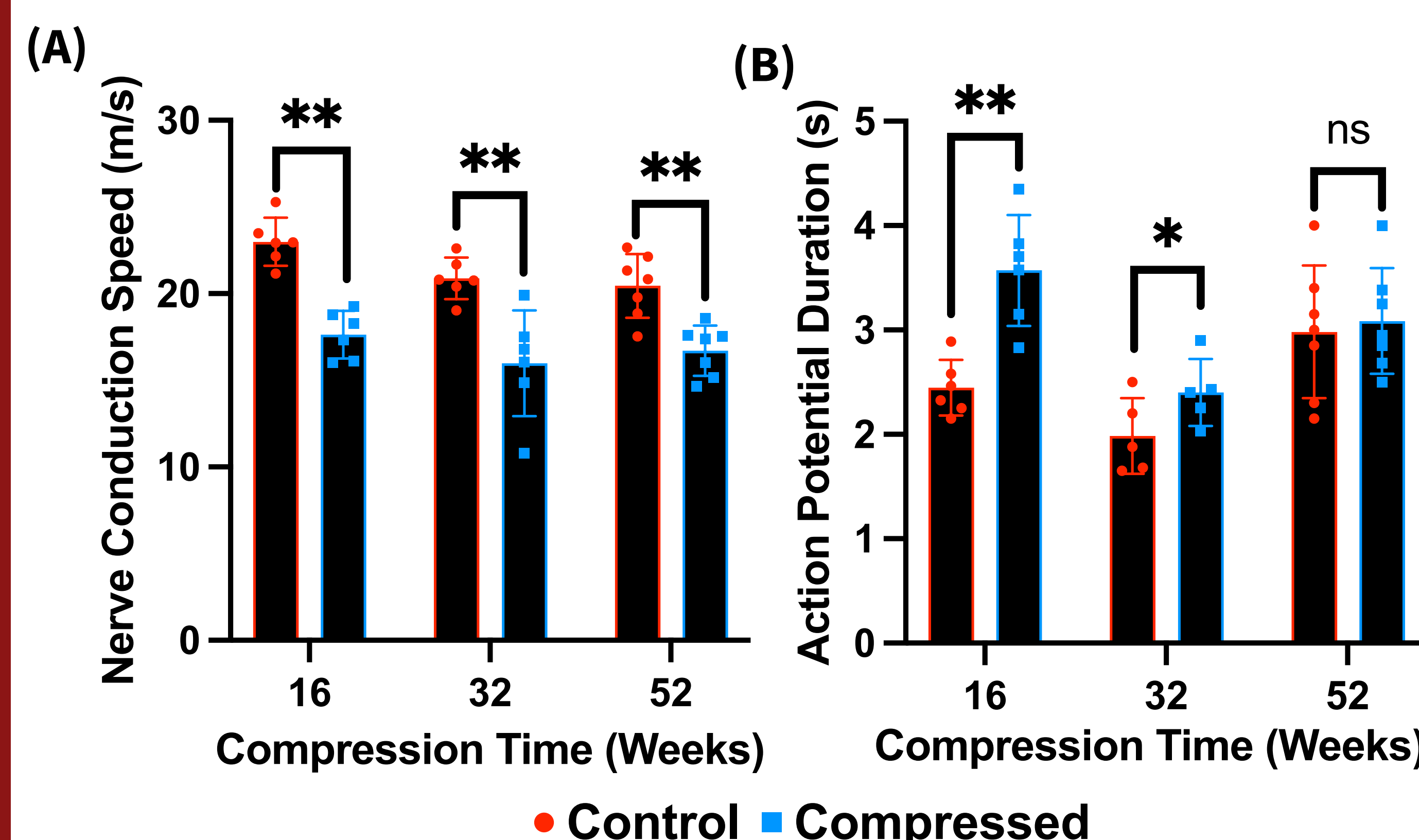


Figure 1: Electrodiagnostic data. **(A)** Decreased nerve conduction velocity at 16w ($p=0.002$), 32w ($p=0.009$), and 52w ($p=0.001$). **(B)** Lengthened action potential duration that normalized over time (16w: $p=0.003$ || 32w: $p=0.03$ || 52w: $p=0.60$).

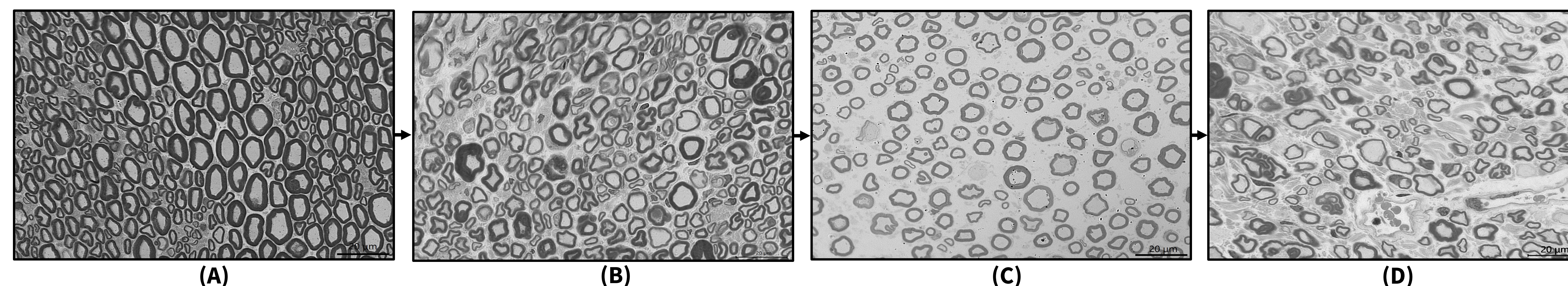
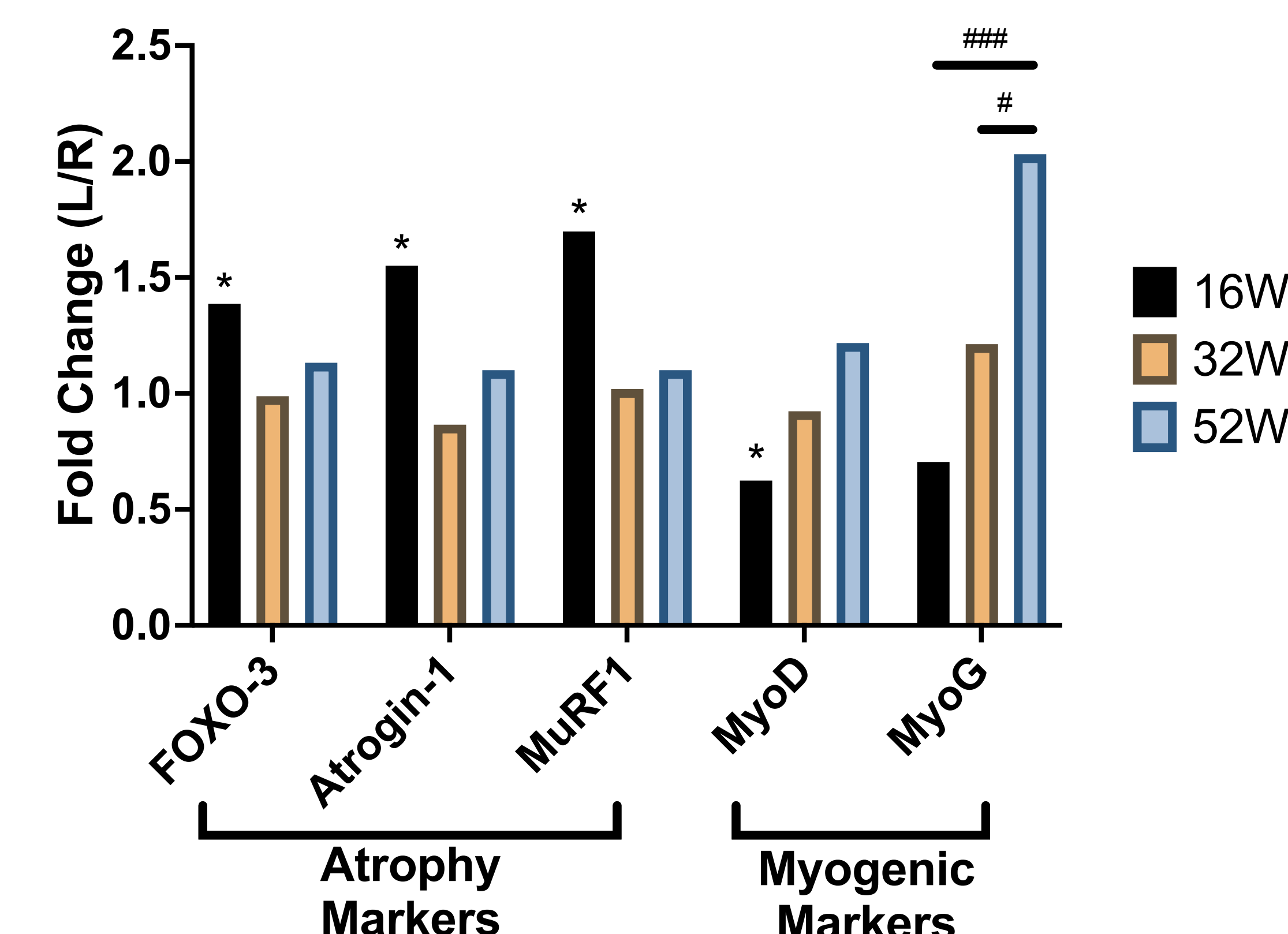


Figure 3: Compared to the **(A)** control group, nerve histology demonstrated a progressive increase in the interaxon space that intensified with longer compression from **(B)** 16 weeks to **(C)** 32 weeks to **(D)** 52 weeks. Mice experienced significant reductions in axon density from 16w to 52w ($p=0.01$) with the most significant reduction, between consecutive timepoints, from 16 weeks to 32 weeks. Total fiber cross sectional area was significantly reduced at 16w ($p=0.009$) and 52w ($p=0.03$).

Figure 2: Muscle PCR Analysis. Increased expression of atrophy genes at 16 weeks (FOXO3: FC=1.39; $p=0.02$ || Atrogin-1: FC=1.55; $p=0.02$ || MuRF1: FC=1.70; $p=0.002$) with a return to baseline by 32 weeks. Myogenic markers were initially decreased at 16 weeks (MyoD: FC=0.62; $p=0.02$ || MyoG: FC=0.70; $p=0.07$). However, MyoG demonstrated increased expression from 16 weeks to 52 weeks (16w: FC=0.75 vs. 52w: FC= 2.1, $p<0.001$) with the most significant increase, between consecutive timepoints, occurring from 32 weeks to 52 weeks (32w: FC=1.241 vs. 52w: FC=2.095, $p=0.02$).



Conclusions

- CNC in a longitudinal murine model of nerve compression causes decreased nerve conduction speeds, reductions in axon density, and changes to axon structure.
- Axonal changes occur between 16 weeks to 32 weeks, with some recovery of nerve function over time.
- Muscular remodeling occurs between 32-52 weeks, with gene expression revealing an initial increase in atrophy markers with a compensatory increase in myogenic markers.

Future Directions

- Evaluate nerve histology proximal and distal to sciatic nerve compression
- Characterize neuromuscular junction morphology to improve understanding of muscle changes