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Critical roles of decompression in functional recovery of ex vivo spinal cord white matter

Laboratory investigation

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Object. The correlations between functional deficits, the magnitude of compression, and the role of sustained compression during traumatic spinal cord injury remain largely unknown. Thus, the functional outcome of this type of injury with or without surgical intervention is rather unpredictable. To elucidate how severity and duration of compression affect cord function, the authors have developed a method to study electrophysiological characteristics and axonal membrane damage in white matter from guinea pig spinal cord.

Methods. Ventral white matter strips isolated from adult guinea pigs were compressed by a compression rod at a level of either 60 or 80% and held briefly, for 30 minutes, or for 60 minutes. In half the experimental groups, a decompression phase consisting of probe withdrawal and 30 minutes of recovery was also applied. For all cord samples, functional response was continuously monitored through compound action potential (CAP) recording. In addition, axonal membrane damage was assessed by a horseradish peroxidase (HRP) exclusion assay.

Results. After 30 minutes of sustained compression at levels of 60 or 80%, a spinal cord decompression procedure caused a significant CAP recovery, with specimens reaching 97.5 ± 6.84% ($p < 0.05$) and 56.2 ± 6.14% ($p < 0.05$) of preinjury amplitude, respectively. After 60 minutes of compression, the amount of CAP recovery following the decompression stage was only 65.5 ± 9.33% for 60% compression ($p < 0.05$) and 29.8 ± 6.31% for 80% compression ($p < 0.05$). Unlike the CAP response, HRP uptake did not increase during sustained compression, and the data showed that HRP staining was primarily time dependent.

Conclusions. The degree of axonal membrane damage is not exacerbated during sustained compression. However, the electrical conductivity of the cord white matter weakens throughout the duration of compression. Therefore, decompression is a viable procedure for preservation of neurological function following compressive injury.
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KEY WORDS • computational modeling • finite element analysis • horseradish peroxidase • spinal cord injury

COMPRESSION is the predominant mode of damage in traumatic SCI.[2,23] In such cases, immediate surgical decompression is often recommended, even though this technique does not always result in complete functional recovery. Papadopoulos and colleagues[25] have found that, in patients with compressive SCI, decompression within 24 hours after the initial insult leads to significant functional recovery compared with decompression performed between 48 hours and 2 weeks after injury. However, even though clinical evidence has shown that early decompression is beneficial to neurological outcome in patients with acute SCI, surgical decompression is only considered as a "practice option."[8,10,11,18] Indeed, conflicting data from McKinley and colleagues[21] showed no significant difference in functional recovery between cases in which surgery was performed early (< 24 hours) or late (> 72 hours) or not performed at all. In addition, Vacarro et al.[40] obtained similar data, with no improvement in spinal recovery in patients undergoing immediate (< 3 days) or delayed (> 5 days) decompression. The controversy over the optimal intervention time may be explained by additional factors, including the severity of the initial trauma. The damage intensity certainly affects

Abbreviations used in this paper: CAP = compound action potential; FEA = finite element analysis; HRP = horseradish peroxidase; SCI = spinal cord injury.

This article contains some figures that are displayed in color online but in black and white in the print edition.

functional recovery, but the coupling between injury duration and magnitude is unclear.

Studies with current animal injury models have begun to elucidate the role of individual factors such as nominal compression,[3,5] duration,[6,7] or the combination of the two[38] in SCI. However, a physiological basis for choosing optimal intervention times for decompression is still lacking. Additionally, it is difficult to foresee the functional benefits to injured spinal cord from surgical decompression. Therefore, the goal of this study was to probe the direct relationship between mechanical forces and neurological outcomes in SCI decompression. Specifically, we wanted to observe the real-time tissue response after decompression as a function of time and injury magnitude. To address these questions, we have developed a novel system that can simultaneously record nominal compression and the concurrent functional response of spinal cord ex vivo. Using this acute animal model, we are able to study the role of the magnitude and duration of compression, as well as the ramifications of decompression as it pertains to functional and anatomical outcomes.

Methods

Isolation of Ventral White Matter From Guinea Pig Spinal Cord

A total of 30 guinea pigs with body masses of 250–350 g were used in this study. The experimental procedures were similar to those of previous studies[19,30–32,37] and were approved by the Purdue University Animal Care and Use Committee. First, the animal was anesthetized (ketamine 60 mg/kg and xylazine 10 mg/kg) and perfused with cold oxygenated Krebs solution. The vertebral column was then removed, and a complete laminectomy was executed. Next, the spinal cord was carefully extracted with microscissors and isolated by cutting longitudinally along the medial sagittal plane. Ventral white matter strips were separated by cutting each half cord radially (Fig. 1A). To maximize tissue viability, the ventral white matter sections were immediately stored in oxygenated Krebs solution for at least 1 hour before further testing.

Sustained Compression of Ventral White Matter and Electrophysiological Recording

Compressive deformation of ventral white matter strips was performed using a procedure similar to that previously reported.[24] A standard sucrose gap recording device[30–32,37] was implemented into a novel soft tissue tester (Fig. 1B and D). A 4-cm-long ventral white matter strip was placed across the sucrose gap chamber with the middle cord positioned in the central compartment of the chamber while its 2 free ends rested in the side compartments. The central compartment was perfused with oxygenated Krebs solution maintained at 37°C, while the 2 side compartments were filled with isotonic (120 mM) KCl. Two gaps, each located between the central and side compartments, were perfused with sucrose (320 mM) to avoid ion exchange between the central and side compartments. To prevent solution leakage between chambers, the ventral white matter strip was sealed with vacuum grease and thin pieces of plastic on both sides of the sucrose gaps. The cord sample in one end of the chamber was stimulated, and the corresponding CAPs were recorded from the other end via Ag-AgCl wire electrodes. Stimuli were carried in the form of 0.1-msec constant current unipolar pulses every second. Recordings were obtained at 1-Hz frequency with a Neurocorder (Neurodata Instruments Corp.) interfaced to LabVIEW (National Instruments).

During the compressive deformation, the white matter strip was placed on the tissue holding stage (located in the central compartment of the sucrose gap chamber), and the compression rod was lowered gradually until it contacted the cord. The lowering was monitored with the aid of a computer and LabVIEW software. The thickness of the cord strip was determined as the distance from the tip of the compression rod to the surface of the tissue holding stage. Each tissue sample was first compressed at a rate of 0.05 mm/second to either of 2 levels: 60 or 80% compression—that is, 40 or 20% of the original thickness, respectively (Fig. 1C). In one scenario, compression was immediate (no sustained compression). In the other 2 cases, compression was maintained at the respective deformation level for either 30 or 60 minutes. To investigate the functional recovery after a decompressive procedure, the CAP response was monitored for an additional 30 minutes after the compression rod was removed from the tissue.

Digital Imaging and Analysis of HRP-Stained White Matter Sections

The HRP exclusion test procedures were similar to those used in previous studies.[29,33,37] Immediately after compression testing and electrophysiological recording, the ventral white matter strips were stored for 1 hour in an oxygenated Krebs solution containing 0.015% HRP. The strips were fixed in 2.5% glutaraldehyde for an additional 1.5 hours, and then 30-μm transverse sections were cut from the injured site of the strips using a vibratome. Cord sections were processed with diaminobenzidine to reveal the extent of HRP uptake by damaged axons. Digital images of the HRP-stained cord sections were obtained using a personal computer connected to an optical microscope. The transverse cross-section of the ventral white matter was divided into 3 subregions of equal width (Fig. 1C). The medial region (M) represented the innermost area of the white matter. The intermediate region (I) was made up of the middle zone, and the lateral area (L) consisted of the outermost white matter. The stained axons in each subregion were counted, and the result was expressed as a density (axons/mm^2) or percentage. In percentage calculation, the value of 4300 axons/mm^2 was used for normalization, as this value approximates the maximum density of damaged axons permeable to HRP found in guinea pig ventral white matter.[34]

Finite Element Analysis

A plane strain finite element model of the guinea pig spinal cord ventral white matter was previously developed.[13] The compressible form of the Mooney Rivlin hyperelastic strain energy function was developed in COM-

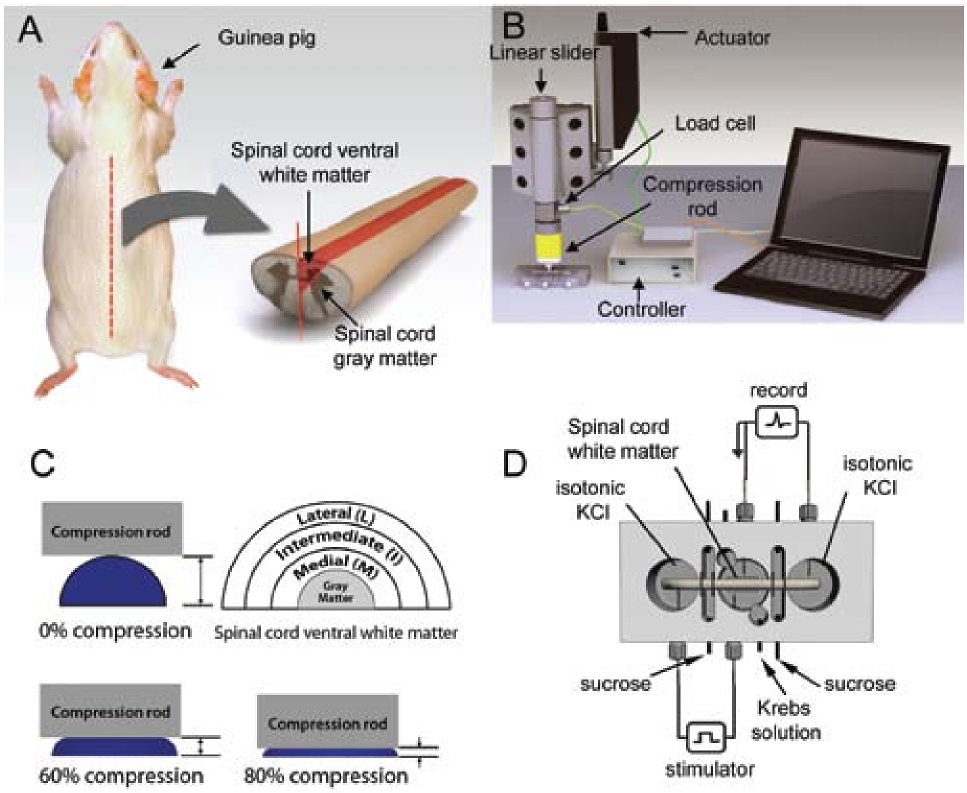


Fig. 1. Diagram showing isolation of ventral white matter and the multimodal measuring system. A: The whole spinal cord was isolated from guinea pig, and the ventral white matter was collected by cutting the half cord as shown. B: Composite image illustrating the setup for inducing compressive injury. The cord samples were compressed by means of a soft tissue tester monitored through a computer. An actuator was coupled to a linear slider, which was in turn attached to a load cell. A rectangular compression rod made of Teflon was attached to the load cell bottom. Electrophysiological response was recorded concurrently with compression. C: Diagram showing a transverse view of a ventral white matter strip and 0, 60, or 80% nominal compression. D: Diagram *(top view)* of the sucrose gap recording chamber. Isotonic sucrose solution was perfused through the gaps to separate isotonic KCl and oxygenated Krebs solution. Electrical stimuli were triggered at left side of the sucrose gap chamber and CAPs were recorded at the opposite side.

SOL 3.2 with Matlab (COMSOL, Inc.). In simulating the force response during stress relaxation, a linear Maxwell element was used.[12] After the initial ramp to 60 or 80% nominal compression, the stress was assumed to decay according to,

$$\sigma = (\sigma_0 / 2) \times [e^{(-t/\tau_1)} + e^{(-t/\tau_2)}]$$

where t was the relaxation time, σ_0 was the peak stress, and τ_1 and τ_2 were the relaxation time constants. The value of τ_1 was taken to be the one at which the force relaxed to $0.3679F_0$ and the second relaxation time constant (τ_1) was determined by numerically minimizing the difference between the experimental force measurement and the predicted force history. The von Mises stress contours were generated at nominal compression levels of 60 and 80% strains.

Statistical Analysis

A 1-way ANOVA with Tukey post hoc test was used in the data analysis for comparisons. In addition, a Student t-test was also used for appropriated pairings. In both instances, probability values < 0.05 were considered statistically significant. All data are presented in the form of means ± standard errors.

Results

Real-Time Recording of Force and Electrophysiological Measurements

The soft tissue tester was implemented with a sucrose gap recording chamber that allowed concurrent recording of deformation, force, and electrophysiological characteristics in a single sample (Fig. 1). Examples of force profiles of ventral white matter strip at 60 or 80% compression for 30 and 60 minutes are depicted in Fig. 2. Four force profiles revealed that the force exerted on the sample reached the peak value at the end of the ramp phase and relaxed immediately to a steady-state force (about 0.01 N). The peak force in samples compressed to 80% compression for either 30 or 60 minutes had similar magnitudes. However, the peak forces of samples compressed to 60% were about half the magnitude of the 80% compressed groups. Reduced compression resulted in lower peak force applied to the sample, regardless of compression duration.

TABLE 1: Compound action potential amplitude for white matter compressed briefly, for 30 minutes, or for 60 minutes at 60 and 80% compression*

	60% Compression		80% Compression			
Duration	Amplitude (%)	No. of Specimens	Amplitude (%)	No. of Specimens	p Value	Decompression
brief	91.0 ± 0.85	5	63.4 ± 4.62	5	<0.001	no
brief	98.2 ± 2.27	5	85 ± 2.43	5	<0.01	yes
30 min	43.15 ± 6.73	9	7.29 ± 1.61	10	<0.001	no
30 min	97.5 ± 6.84	4	56.2 ± 6.14	5	<0.01	yes
60 min	29.73 ± 4.23	12	4.57 ± 1.86	7	<0.001	no
60 min	65.5 ± 9.33	7	29.8 ± 6.31	5	<0.05	yes

* The CAP amplitude was normalized as the percentage of the preinjury value. Higher CAP amplitude means less functional damage. The CAP amplitude at 60% compression was compared with that measured at 80% compression for each mechanical condition (brief, 30-min, or 60-min duration with or without decompression) by Student t-test.

Dependence of Functional Deficit and Recovery on Nominal Compression and Duration

The CAP is the spatiotemporal sum of nerve action potentials and, in terms of electrophysiology, a higher CAP amplitude translates into less functional damage.[31] This study revealed that the CAP amplitude was significantly higher at 60% compression than at 80% compression in all pairwise comparisons (Table 1). Immediately after brief compression (no sustained compression), the CAP amplitude was 91.0 ± 0.85% for 60% compression (5 specimens) and 63.4 ± 4.62% for 80% compression (5 specimens). After 30 minutes of sustained compression, the CAP amplitude was 43.15 ± 6.73% for 60% compression (9 specimens) and 7.29 ± 1.61% for 80% compression (10 specimens; $p < 0.01$). After 60 minutes of sustained compression, the CAP amplitude was even lower, down to 29.73 ± 4.23% for 60% compression (12 specimens) and 4.57 ± 1.86% for 80% compression (7 specimens). The decreasing CAP trends are evident in Fig. 3, as the CAP traces show a marked conduction dysfunction dur-

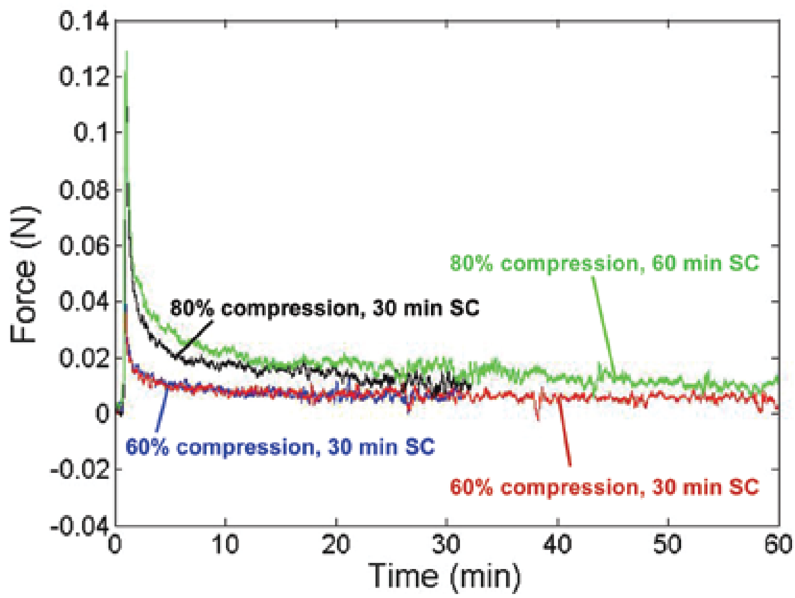


Fig. 2. Graph showing an example of the force profiles of ventral white matter strips compressed to 60 or 80% for 30 or 60 minutes. Force generated on the samples reached peak values within a minute after compression started and relaxed immediately to steady state. All 4 samples had steady-state forces converged to similar magnitude (0.01 N). SC = sustained compression.

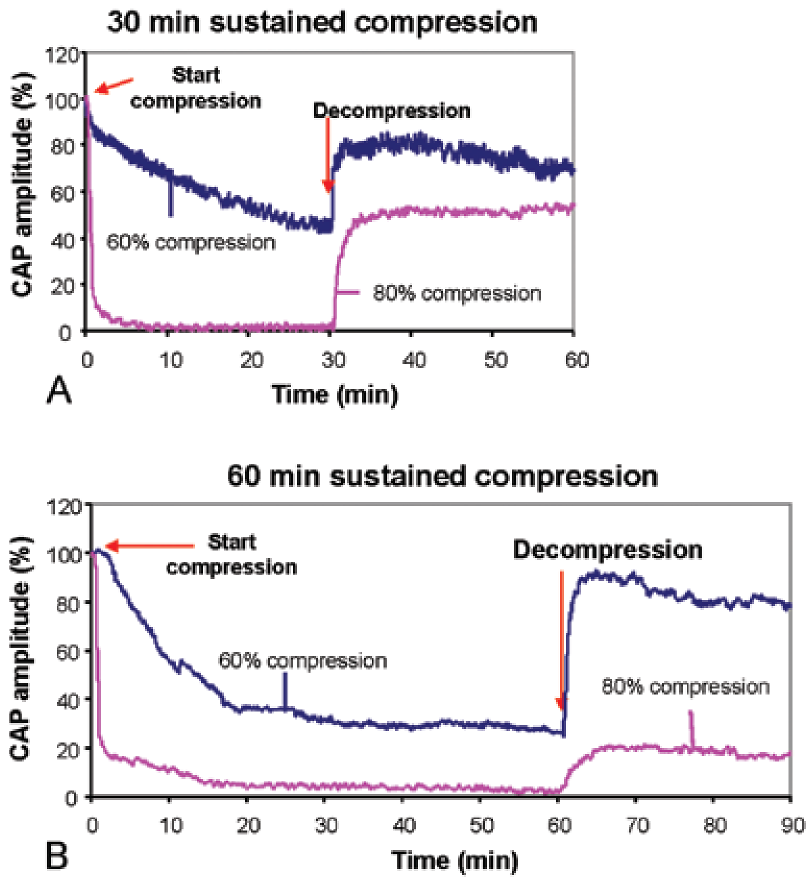


FIG. 3. Graphs showing examples of CAP profiles of ventral white matter strips with sustained compression and decompression. Samples were compressed to 60 or 80% for 30 minutes (A) or 60 minutes (B). After decompression, CAP was continuously monitored for 30 minutes. During sustained compression CAP kept declining. Recovery of CAP occurred immediately after decompression, but the magnitude did not reach a preinjury level.

ing applied loading. The results of statistical comparison between the compression duration and corresponding CAP changes are listed in Table 2.

Meanwhile, a decompression procedure (compression rod retraction with 30-minute recovery) resulted in significantly higher CAP responses than in groups without decompression (Table 3). By allowing decompression with an additional 30-minute rest, the briefly compressed tissue recovered to 98.2 ± 2.27% for 60% compression (5 specimens) and 85 ± 2.43% for 80% compression (5 specimens). Even with 30 minutes of sustained compression, performing decompression caused a CAP increase approaching 97.5 ± 6.84% for 60% compression (4 specimens) and 56.2 ± 6.14% for 80% (5 specimens). With 60-minute duration of compression, decompression caused the CAP to recover to 65.5 ± 9.33% for 60% compression (7 specimens) and 29.8 ± 6.31% for 80% compression (5 specimens). Note that the CAP stabilized within a few minutes after the probe was withdrawn (Fig. 3). The data show the degree of CAP recovery to be inversely proportional to the magnitude and duration of compression.

Axonal Membrane Damage and Effect of Initial Impact

As opposed to CAP response, the experimental results show axon membrane damage was not worsened during sustained compression (Fig. 4). In specimens that were immediately compressed, the corresponding HRP uptake was 11.3 ± 1.26% at 60% compression (4 specimens) and 25.9 ± 8.15% for 80% compression (5 specimens, Table 4). After 30 minutes of sustained compression, the HRP uptake declined to 2.8 ± 0.40% for 60% compression (5 specimens) and 7.3 ± 1.43% for 80% compression (5 specimens). After 60 minutes of sustained compression, the HRP uptake was 2.26 ± 0.58% for 60% compression (4 specimens) and 5.1 ± 1.26% for 80% compression (4 specimens). The decreasing HRP trend indicates axonal recovery had already commenced while the cord was being compressed. With additional decompression and 30 minutes of recovery, HRP staining was 1.1 ± 0.31% in 60% (5 specimens) and 2.4 ± 0.74% in 80% (5 specimens) briefly compressed groups. Similarly, in samples undergoing sustained compression for 30 minutes, HRP uptake after decompression was 1.9 ± 0.87% in 60% compression (5 specimens) and 4.9 ± 1.1% for 80% compression

TABLE 2: Results of statistical comparison between compression duration and corresponding CAP changes*

Compression (%)	Duration Comparison			Decompression
	Brief vs 30 min	Brief vs 60 min	30 vs 60 min	
60	p<0.001	p<0.001	NS	no
60	NS	p<0.05	p<0.05	yes
80	p<0.001	p<0.001	NS	no
80	p<0.01	p<0.001	p<0.05	yes

* A 1-way analysis of variance was used to compare the CAP amplitude with compression of brief, 30-min, and 60-min durations at each condition (with 60 or 80% compression with or without decompression). In each condition, there was a significant difference among the 3 duration groups. The Tukey-Kramer multiple comparison test was used to further investigate which pairs of comparison yield significant difference. Abbreviation: NS = not significantly different.

(5 specimens). Only cords compressed for 60 minutes differed significantly in HRP labeling, with the percentage of axons labeled after decompression at 1.2 ± 0.07% for 60% (4 specimens) and 3.8 ± 0.48% for 80% groups (6 specimens, $p < 0.01$).

Spatial Distribution of Axon Damage and Correlation With Steady Force After Stress Relaxation

Simulation of stress relaxation using FEA showed that there was no statistical difference between the relaxation time constants (τ_1 and τ_2) for transverse compression at 60 and 80% nominal compression (Fig. 5). The von Mises stress (σ_{vm}) distribution of the transverse ventral white matter immediately after compression and as a function of time was generated from an FEA model for both 60 and 80% injury levels (Fig. 4A–D). The predicted stress distribution produced by the computational model was compared with the local distribution of axonal damage revealed by HRP staining in both compression groups (Fig. 4E–H). In all simulations, the von Mises stress immediately after compression was the highest in the medial region and the lowest in the lateral region. Moreover, the 80% compression group had a higher von Mises stress profile and HRP uptake than the 60% compression group. After 60 minutes of sustained compression, the stress was uniformly low across the ventral white matter in the 60 and 80% compression groups. However, there was still significant HRP staining in the medial region, especially at 80% compression. A possible explanation for such inconsistency was that axonal membrane damage was initiated by initial deformation, and membrane resealing occurred throughout the compression phase. However, the rate of resealing was much slower than the rate of stress relaxation. In fact, the time profile of von Mises stress showed that stress relaxed quickly (Fig. 5). Up to 60 seconds after the sample was compressed to 60 or 80%, the residual stress was < 3 kPa from the 22 kPa maximum. Therefore, the predominant damage incurred within the cord was due to the initial traction.

Further, numerical comparisons between the initial von Mises stress and the HRP staining (immediately after brief compression) at the global and local tissue scale were made. We plotted the relationship between the von Mises stress and percentage of HRP uptake observed in the medial, intermediate, and lateral subregions of white matter at both 60 and 80% compression (Fig. 1C). The relationship tended to be linear, with a regression line of $y = 3.1565x - 6.0908$ ($R^2 = 0.8043$, $p < 0.05$; Fig. 6).

Discussion

Stress Relaxation in Spinal Cord Tissue

Biological tissues are generally viscoelastic (that is, their mechanical response is rate dependent and they show stress relaxation at a constant strain level), anisotropic (due to their specific arrangement of microstructure), and nonlinear.[14] A full characterization of the constitutive behavior can be studied via different loading schemes including shear, uniaxial tension, and compression. In the

TABLE 3: Comparison of CAP amplitude with and without decompression*

Compression (%)	Decompression vs No Decompression	Duration
60	p<0.05	brief
60	p<0.001	30 min
60	p<0.001	60 min
80	p<0.01	brief
80	p<0.001	30 min
80	p<0.05	60 min

* The Student t-test was used to compare the CAP amplitude with and without decompression at each condition (with 60 or 80% compression with brief, 30-min, or 60-min duration of compression). There was a significant difference in all pair-wise comparisons.

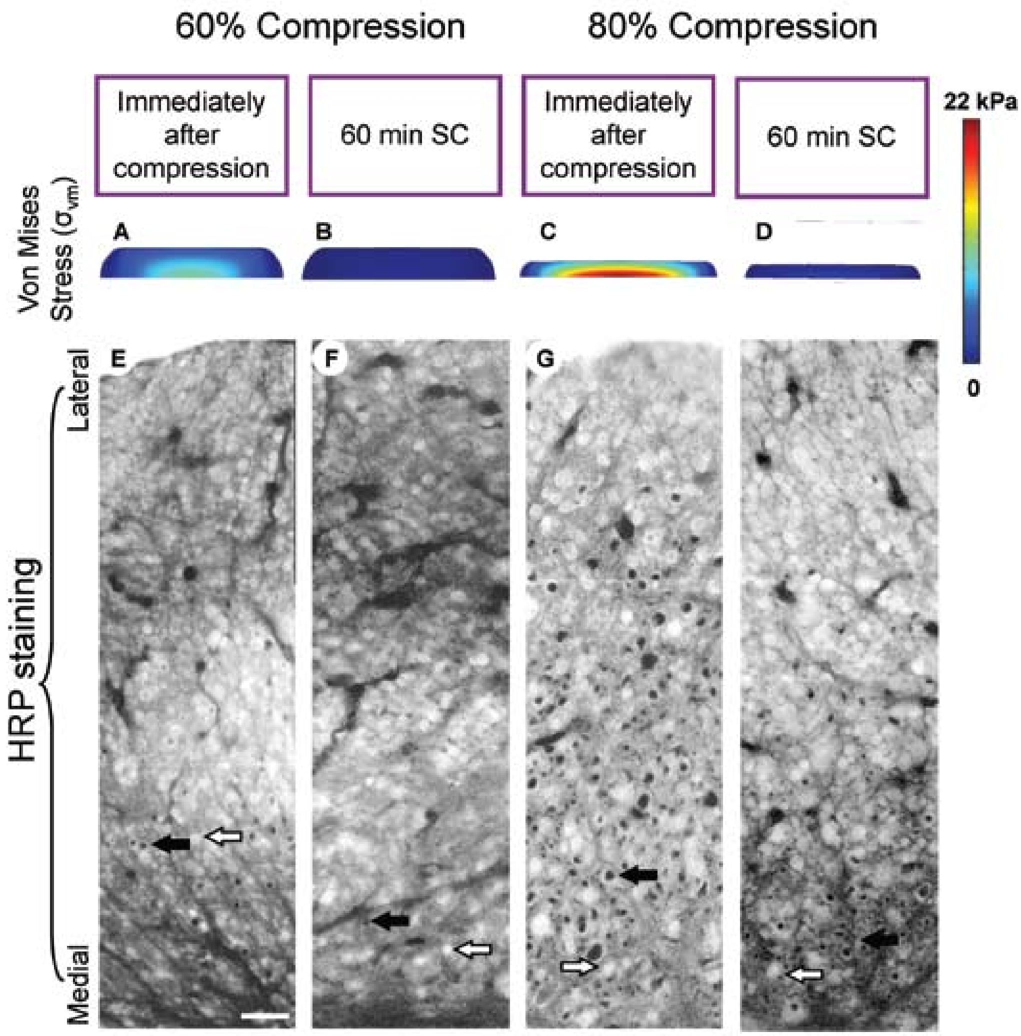


FIG. 4. Photomicrographs of stained white matter sections demonstrating (HRP) labeling and the corresponding von Mises stress (σ_{vm}) profiles (as predicted by FEA). A–D: Von Mises stress maps with brief and 60-minute compression at 60 and 80%. E–H: Image of HRP staining in the center portion of a transverse section of ventral white matter. For all images, the *open arrows* indicate undamaged axons, whereas the *darkened arrows* indicate axons stained with HRP. Bar = 15 μm (E–H).

present study, the viscoelastic characteristics were determined by stress relaxation experiments. Real-time force recording in spinal cord white matter strips in sustained compression displayed a characteristic relaxation behavior in quasistatic compression (0.05 mm/second). In spinal cord tissue, the force recovered quickly, with the relaxation time lasting less than a minute.[12] This recovery time is much shorter than that observed in many other biological tissues such as ligaments[16] and tendons.[20] Force recovery in such a short period may be explained by the tissue's high water content, which can range between 70 and 75% in a healthy spinal cord.[22] The high water volume may facilitate axon rearrangement after compression, allowing the force experienced in each axon to decrease markedly. Once the axons have reassembled and adapted to the new environment, self-recovery mechanisms, such as membrane resealing, may be initiated.[30,35,36,39]

Functional Deficit Depends on the Nominal Compression and Duration of Sustained Compression

The CAP is a measurement of electrophysiological conductivity of axons and is therefore a metric for biological function in spinal cord. Sustained compression in spinal cord ventral white matter strips resulted in a continuous decline in CAP amplitude, indicating that the physical environment of the tissue sample was changed. Not surprisingly, higher nominal compression also led to further CAP decreases and irreversible functional deficit.

In several clinical reports, surgical decompression has been shown to relieve damage in injured spinal cord and promote functional recovery in clinical and animal studies.[9,15,25] Our ex vivo study demonstrates that relief from sustained compression corresponded to an almost immediate improvement in the functional response. Indeed, even after 1 hour of sustained compression at 60%

TABLE 4: Percentage of HRP uptake after brief, 30-minute, and 60-minute sustained compression at 60 and 80%*

Duration	60% Compression HRP Uptake (%)	60% Compression No. of Specimens	80% Compression HRP Uptake (%)	80% Compression No. of Specimens	Decompression
brief	11.3 ± 1.26	4	25.9 ± 8.15	5	no
brief	1.1 ± 0.31	5	2.4 ± 0.74	5	yes
30 min	2.8 ± 0.40	5	7.3 ± 1.43	4	no
30 min	1.9 ± 0.87	5	4.9 ± 1.1	5	yes
60 min	2.26 ± 0.58	4	5.1 ± 1.26	4	no
60 min	1.2 ± 0.07	4	3.8 ± 0.48†	6	yes

* The HRP uptake was normalized as percentage of maximum axons permeable to HRP (4300 axons/mm^2). Higher HRP uptake denotes more axonal membrane damage. The HRP uptake at 60% compression was compared with that at 80% for each condition by means of Student t-test (with brief, 30-min, or 60-min duration with or without decompression). There was a significant difference only in samples compressed for 60 mins and with decompression.

† $p < 0.01$.

magnitude, the CAP was restored to 66 ± 9.33% of preinjury values after a decompression procedure (Table 1). Because CAP recovery is also injury-level dependent, it is expected that milder forms of insult would see an even greater rebound in electrophysiological conductivity. Thus, from an acute injury perspective, decompression has beneficial physiological implications. This observation also helps explain why surgical decompression does not always result in functional recovery in SCI patients, because the degree of injury varies among patients. In addition, the time scale between initial trauma and surgical decompression is also inconsistent. Because spinal cord conduction decreases as a function of injury duration, the impetus for immediate decompression is also evident.

Membrane Resealing in Damaged Axons During Sustained Compression

In contrast to the findings with respect to CAP, damaged axonal membranes seemed to possess a self-recovery mechanism during sustained compression. Membrane damage revealed by HRP uptake was the most severe immediately after brief compression, whereas staining was significantly less in groups of specimens compressed for 30 or 60 minutes (with or without decompression). Thus, membrane resealing of damaged axons occurs even during applied compression. Because the CAP response continued to decline during sustained compression, the collective data imply that membrane integrity is necessary but not sufficient for proper axon conduction. Prior reports have shown compression to induce physical environment changes within the cord, such as intra- and extracellular ionic imbalance and dislocation of the myelin sheath surrounding the axons.[1,17] The current findings are therefore consistent with the notion that additional disruptions at the cellular level may alter axon conductivity even when the membrane is intact.

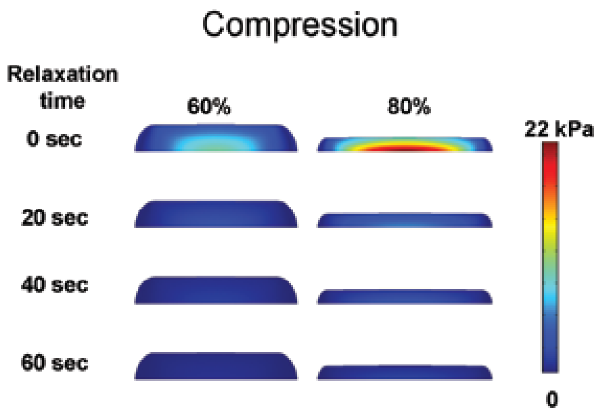
The results of HRP staining were also in good agreement with the simulated von Mises stress distributions immediately after applied compression. This finding provides further corroboration for von Mises stress as a possible metric for damage analysis.[24] The von Mises stress predicted by the FEA model reached the peak immediately when the cord was compressed to 60 or 80% and decreased instantaneously afterward during stress relaxation. Similarly, the HRP uptake was highest immediately after brief compression and decreased markedly even after 30 or 60 minutes of sustained compression. This result indicates that axonal membranes were primarily damaged by the initial impact of compressive injury. Once the stress experienced by axons decreases, a "molecular memory" of the axons might induce membrane resealing that allows axons to "recover" to their original structure.[39] Therefore, during stress relaxation when the stress is decreasing asymptotically, the membranes are resealing with minimum mechanical restriction. The time frame of membrane resealing is also consistent with previous observations.[30,35] The current data, however, also show that membrane sealing occurs in the presence of compression.

Limitations of the Current Model

This study focused on the primary injury of spinal cord white matter in an ex vivo unconfined preparation. The emphasis of our research is focused on the acute tissue response in addition to concurrent force and electrophysiological and axonal membrane measurements before and after decompression. The effects of secondary injury, including the hemodynamic response, have not been studied. Indeed, later events such as Wallerian degeneration and demyelination might be responsible for the irreversible functional loss after decompression.[4,7,26–28] Such phenomena should be further investigated in future studies that link mechanical trauma to secondary cascades in compressive SCI.

Conclusions

In the current study, we show, for the first time, the connection between sustained mechanical trauma and the neurological response via concurrent measurement of force and electrophysiological function in the same speci-



Nominal Compression	τ_1 (s)	τ_2 (s)
60% (n = 32)	3.8 ± 1.9	28.9 ± 6.8
80% (n = 27)	4.3 ± 1.5	32.7 ± 5.6

FIG. 5. Von Mises stress maps showing the time profile of von Mises stress in transverse cross-section of ventral white matter strip at 0, 20, 40, and 60 seconds after the strip was compressed to 60 or 80%. There was no statistical difference between the relaxation time constants (τ1 and τ2) for transverse compression at 60 and 80% compression. n = number of cord specimens; s = seconds.

men. We have found that during sustained compression, no additional membrane damage is incurred at the prescribed compression levels. However, during continuous compression, the conductivity of the spinal cord is impaired. Therefore, surgical decompression appears to be beneficial for preserving neurological function in early-stage compressive injury.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

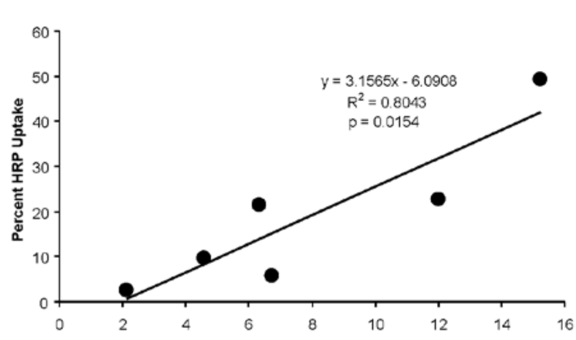


FIG. 6. Graph showing correlation between the average of HRP uptake percentage with brief duration of compression at 60% and the corresponding von Mises stress at medial, intermediate, and lateral subregions of white matter. The y refers to HRP staining (%), whereas x refers to von Mises stress.

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