The characterization of age-related differences in inflammatory and behavioral responses following spinal cord contusion in rats

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Objective/Aim/Hypothesis:
The damage that results from spinal cord injury (SCI) is caused by both the initial mechanical trauma and the secondary injury that exacerbates the inflammatory reaction at the lesion site. As the average age at which an individual suffers an SCI has increased over the past decades, it has become increasingly relevant to determine what role age has on that inflammatory response. The aging process has been thought to be coincident with a state of nonresolving activation of inflammatory pathways, but many studies that have investigated the role of aging and SCI have found mixed results. Due to the modulation of the inflammatory response with age, we hypothesized that the different level of dysfunction observed in differently aged animals would correlate with the variability in the level of inflammation.

Design/Approach/Methods:
Female Sprague-Dawley rats of three different age groups (2-3 months, 5-6 months, and 10-12 months) received a laminectomy at the 9th thoracic vertebral level (T9) followed by a 200 kilodyne contusion injury with the Infinite Horizon Impactor. Uninjured control rats received a laminectomy at T9. All animals received identical post-operative care. Rats were sacrificed at either 7 or 42 days following surgery. Motor, sensory, and autonomic function were assessed prior to injury and at regular intervals until sacrifice, at which point the injury epicenter was dissected, dissociated, and analyzed by flow cytometry for inflammatory markers. Following sacrifice, μCT of the femurs was performed using a Scanco Medical μCT50 device at 70kVp. Repeated functional measures were analyzed using a mixed model test; cytometric data was analyzed using a two-way ANOVA. Linear regressions were used to determine the correlation between inflammation and sensory dysfunction and bone loss.

Results:
Both hindlimb motor function and urinary retention displayed injury-induced impairment, but neither showed age-related differences in recovery of function. Sensory dysfunction was still evident in all injured groups studied at 6 weeks following injury ($p<0.05$). Micro CT analysis revealed significant bone loss with age and following SCI ($p<0.05$). The level of inflammation observed in the spinal cord injury epicenter was elevated with respect to control animals from all age groups and at all time points, though there was no effect of age on the inflammation of injured rats at either 7 or 42 days post injury. Strikingly, the level of inflammation at the injury epicenter is correlated with both the development of allodynia and the degree of bone loss in the femurs at 6 weeks following injury.

Conclusion:
The data suggests that the inflammatory response to contusive spinal cord injury remains consistent regardless of the age at which the animals are injured, from youth to middle-aged. Similarly, the recovery of motor, sensory, and autonomic dysfunction appears to show little variation based on age. The correlation between the degree of an animal's hindlimb bone loss or allodynia to the inflammation at the SCI epicenter, however, demonstrates the pivotal role that inflammation plays in these understudied, secondary complications of spinal cord injury.