Compression Decreases Anatomical and Functional Recovery and Alters Inflammation after Contusive Spinal Cord Injury

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Experimental models of spinal cord injury (SCI) typically utilize contusion or compression injuries. Clinically, however, SCI is heterogeneous and the primary injury mode may affect secondary injury progression and neuroprotective therapeutic efficacy. Specifically, immunomodulatory agents are of therapeutic interest because the activation state of SCI macrophages may facilitate pathology but also improve repair. It is unknown currently how the primary injury biomechanics affect macrophage activation. Therefore, to determine the effects of compression subsequent to spinal contusion, we examined recovery, secondary injury, and macrophage activation in C57/BL6 mice after SCI with or without a 20 sec compression at two contusion impact forces (50 and 75 kdyn). We observed that regardless of the initial impact force, compression increased tissue damage and worsened functional recovery. Interestingly, compression-dependent damage is not evident until one week after SCI. Further, compression limits functional recovery to the first two weeks post-SCI; in the absence of compression, mice receiving contusion SCI recover for four weeks. To determine whether the recovery plateau is indicative of compression-specific inflammatory responses, we examined macrophage activation with immunohistochemical markers of purportedly pathological (CD86 and macrophage receptor with collagenous structure [MARCO]) and reparative macrophages (arginase [Arg1] and CD206). We detected significant increases in macrophages expression of MARCO and decreases in macrophage Arg1 expression with compression, suggesting a biomechanical-dependent shift in SCI macrophage activation. Collectively, compression-induced alterations in tissue and functional recovery and inflammation highlight the need to consider the primary SCI biomechanics in the design and clinical implementation of immunomodulatory therapies.