Age as a Key Determinant of Inflammatory Response, Glial and Axonal Survival After Traumatic Spinal Cord Injury

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Introduction

Aging is a process that results in a progressive reduction of reserves in most physiologic systems and an increasing susceptibility to most diseases and to death. Despite an increasing incidence of traumatic spinal cord injury (SCI) in the elderly in North America, relatively little has been reported to date regarding the role of age on outcomes after SCI. Given this, an improved understanding of the consequences of age on SCI is required. This study examines whether age at the time of injury is a key determinant for inflammatory response, oligodendroglial apoptosis and axonal survival after traumatic SCI.

Methods

This study includes post-mortem spinal cord tissue from 64 cases of SCI (at cervical or high-thoracic level) and 38 controls cases. Each group was subdivided into younger and elderly individuals (65 years of age or older). Alternating 6-microm sections from 2 to 3 segments caudal to the SCI and age/sex/level-matched segments from controls were stained for: (i) neuroinflammation (neutrophils, macrophages, cytotoxic-T/natural-killer cells, helper/regulator-T cells, B-cell lymphocytes); (ii) apoptotic oligodendrocytes; (iii) axons; (iv) extent of degeneration. The number of cells or axons was counted in the motor and sensory areas within the spinal cord using unbiased stereological techniques.

Results

There were 25 women and 77 men with a mean age of 58.6 years (range from 16 to 90 years). Of those, 53 individuals were elderly who died in the acute (n=20), subacute (n=14) or chronic stage following traumatic SCI (n=10); and there were 15 elderly individuals in the control group. In addition, there were 49 younger individuals who died in the acute (n=14), subacute (n=4) or chronic stage after traumatic SCI (n=8); and 23 younger individuals were included in the control group.

Our analysis on inflammatory response to SCI indicate that younger and elderly individuals had statistically similar number of infiltrated neutrophils, number of activated macrophages, and number of infiltrated lymphocytes within the lateral and anterior corticospinal tracts and posterior column in most of the stages after SCI. Yet, younger individuals showed significantly greater number of B-cell lymphocytes within the lateral corticospinal tracts in the subacute stage after SCI in comparison with elderly individuals.

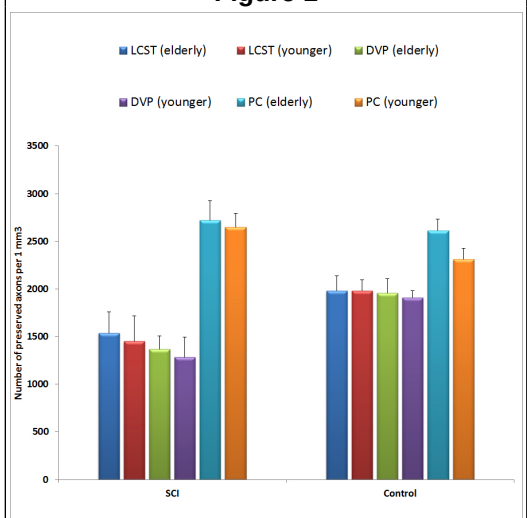
Our analysis of oligodendroglial apoptosis indicate that younger and elderly individuals had statistically similar number of caspase-3+ cells with morphology of oligodendrocytes and similar proportion of Caspase-3+/CC1+ cells within the lateral corticospinal tracts, descending vasomotor pathways and posterior column in all stages after SCI.

Results

The number of preserved axons within the lateral corticospinal tracts, descending vasomotor pathways and posterior column did not significantly differ between younger and elderly individuals with SCI and without CNS injury (Figure 1).

The extend of degeneration within the spinal cord white matter did not significantly differ between the younger and elderly individuals following traumatic SCI.

Figure 1



Comparisons between younger and elderly groups with regard to the number of axons within the lateral cortical spinal tracts (LCST), descending vasomotor pathways (DVP) and posterior column (PC) in cases of SCI as well as in control cases.

Conclusions

Our results indicate that age at the time of injury does not adversely affect the cellular inflammatory response, oligodendroglial apoptosis and axonal survival after traumatic SCI. Those results are consistent with prior clinical studies that have shown no significant effects of age on neurological and functional recovery after SCI when data analysis is adjusted for potential confounders.

References

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Learning Objectives

1) Describe the influence of age at the time of trauma on neuroinflammatory response to SCI, 2) Recognize the effects of age on oligodendrocyte preservation and axonal survival after SCI, and 3) Identify the importance of age as a potential confounder in future translational studies focused on neuroprotective strategies in the management of adults with SCI.