STRUCTURAL AND FUNCTIONAL CHANGES IN NERVE ROOTS DUE TO TENSION AT VARIOUS STRAINS AND STRAIN RATES

INTRODUCTION

Low Back Pain (LBP) occurs in 15-20% of the US population costing $20-50 billion annually (Wheeler, 2002). One of the major sources of LBP and associated radicular pain is chemical irritation, compression or tension on the lumbar roots (Louw, 1986). Compared to compression and irritation, stretch injury of roots has received much less attention. Establishing relationships between root stretch and resulting functional and morphological injuries require detailed investigation. Thus, the specific aims of this study were to determine the following in the nerve roots stretched at various predetermined strains and strain rates: 1) functional changes – changes in the conduction velocity (CV) and area of the evoked compound action potential (CAP), 2) morphological changes – rate of occurrence of hemorrhage, axotomy and impaired axoplasmic transport (IAT) using H&E, silver impregnation, and amyloid precursor protein (β-APP) immunostaining, respectively.

METHODS

Animal Preparation: 56 L5 dorsal nerve roots obtained from 28 adult male Sprague Dawley rats (450-475 g) were used in this in-vivo study. The animals were anesthetized and maintained using ketamine (40 mg/kg, 20 mg/kg, im) and xylazine (5 mg/kg, 2.5 mg/kg, im). An L1-S1 laminectomy was performed and the exposed bilateral L5 nerve roots were cut at the proximal end. All the surgical procedures were approved by the institutional Animal Investigation Committee. Mechanical Testing: An Endura-Tec-3200 (BOSE®, Minnetonka, MN) material testing machine was used to clamp the proximal cut end of the nerve root and tension on the lumbar roots (Louw, 1986). Compared to compression LBP and associated radicular pain is chemical irritation, compression or tension (increased spacing between the axons and torn fibers). The rate of occurrence of these injuries was directly dependent on the applied mechanical condition and increased with increase in strain rate. Thus, axonal injury exhibits strain rate dependency (Fig. 4).

DISCUSSION

Despite the possible role of nerve roots in the etiology of neurologic disorders, limited information is available on the pathomechanisms of nerve root stretch. The current study is the first to establish a direct relation between the applied mechanical condition and the resulting functional and morphological injuries to the nerve roots. Also, since nerve roots are composed mainly of axons, results from the current study should help provide a better understanding of axonal injury mechanisms and tolerance in peripheral and central nervous systems. Finally, this new experimental model could be used to establish a platform for the development of new treatment modalities for the nerve root and other axonal injuries.

RESULTS

Functional Injury: The results indicated that as the strain and strain rate increased, there were significant decreases in CV and area of CAP (Fig. 2A, B). Also, at high strains a complete conduction block (CB) was observed. 16%, 10% and 9% strains were reported to be the thresholds for the occurrence of CB at 0.01 mm/sec, 1 mm/sec and 15 mm/sec strain rates, respectively (Fig. 3). Thus, the axons tolerated a slow stretch better than a fast stretch.

Morphological Injury: Examination of the stretched root sections revealed β-APP accumulation, broken blood vessels and axotomy (increased spacing between the axons and torn fibers). The rate of occurrence of these injuries was directly dependent on the applied mechanical condition and increased with increase in strain rate. Thus, axonal injury exhibits strain rate dependency (Fig. 4).

Figure 1: A: Experimental set up. B: Schematics of the actual test set-up.

Figure 2: Percentage decrease in A) CV and B) Area of the evoked CAP.

Figure 3: Logistic regression analysis of functional injury.

Figure 4: Summary of histological findings in roots when subjected to strains (<10% to >20%) at different strain rates.

Statistical Analysis: One-way ANOVA, linear regression analyses and independent sample t-tests (SPSS, Chicago, IL) were performed to determine how the functional and structural changes were affected by strain and strain rate. In addition, binary logistic regression analyses were performed to determine the threshold for complete functional injury. p < 0.05 was considered significant.