cell-derived neurotrophic factors, slowing axonal regeneration. The inhibitory effect of CSPGs is exercised through tyrosine phosphatase σ (PTPσ) receptor. Intracellular sigma peptide (ISP) is a designer peptide that binds and blocks PTPσ receptor. In a spinal injury model, systemic delivery of this peptide restored substantial serotonergic innervation to the spinal cord below the level of injury and facilitated functional recovery of both locomotor and urinary systems. After ventral root avulsion and immediate reimplantation, modulation of PTPσ by systemic delivery of ISP remarkably enhanced motor neuron regeneration. Given unprecedented effects of ISP in CNS regeneration, the goal of this study was to investigate the effect of ISP on peripheral nerve regeneration.

METHODS: Thirty Lewis rats were used. Both sciatic nerves (20 mm) were harvested from 10 Lewis donors. In the recipient animals, a 10-mm defect was created in the sciatic nerve and the isograft was interposed with 10-0 nylon. The animals were randomized in experimental and control groups. Animals in the experimental group received 100 µg of ISP along the nerve graft on the day of surgery. Animals in the control group received vehicle alone along the nerve graft on the day of surgery. In both groups, the medications were administered subcutaneously once a day following surgery. The investigators were blinded to the administrated medications, until after all outcome measurements were complete. The endpoint of the study was 90 days. Sciatic Function Index (SFI) was measured preoperatively and biweekly after surgery. Nerve conduction latency and amplitude, gastrocnemius muscle weight retention ratio, and histomorphometrical analysis of nerves were performed at endpoint.

RESULTS: SFI declined immediately after surgery, improving gradually with the greatest value dispersion starting at 4 weeks (Graph 1). The average SFI at week 12 was −68 ± 19 in the ISP group and −65 ± 17 in the control group (P = 0.64). The average conduction amplitude was 15 ± 8.6 mV in the ISP group versus 15.9 ± 5.6 mV in controls, whereas conduction latency was 2.5 ± 0.7 ms in the ISP group versus 3.1 ± 2.2 ms in the control group (P = 0.77). The average gastrocnemius muscle weight retention ratio, and histomorphometrical analysis of nerves were performed at endpoint.

CONCLUSION: Daily subcutaneous administration of intracellular sigma peptide did not to significantly improve nerve regeneration at the dose and with the administration route tested.

Histomorphometry in Peripheral Nerve Regeneration: Experimental Comparison of Different Axon Counting Methods

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PURPOSE: Histomorphometry is a common tool to quantitatively evaluate outcomes of peripheral nerve regeneration by measuring axonal parameters such as count, diameter, and myelination. Manual measurement across the entire nerve cross-section is the most accurate technique of histomorphometric analysis but is extremely labor intensive. Thus, most researchers have opted for analysis of just a sample of the cross-section. Currently, automated sampled analysis is the most common method. However, no study has been performed to compare the accuracy of these techniques, making it difficult to compare results across the literature.

METHODS: Rat sciatic nerves were transected and repaired with a 20 mm nerve isograft. A total of 34 sections were stained with toluidine blue and digitized: 24 from native nerve distal to the graft, 5 from nerve proximal to the graft, and 5 from the graft itself. Three blinded researchers manually counted total myelinated fibers in each full cross-section. Total myelinated fiber counts were also extrapolated from sampled fields representing 20% of the cross-sectional area. Sampled counts were performed both manually and automatically with the software ImageJ (National Institutes of Health). Myelinated fiber diameter (FD), axon diameter (AD), and myelin sheath thickness (MTh) were measured manually in the full cross-sections and the sampled fields. Repeated measures MANOVA, Spearman’s correlation, and Wilcoxon signed-rank tests were performed.
RESULTS: Results are expressed in mean ± standard deviation. Full manual axon count was 12,504 ± 4,195 overall and 13,506 ± 4,217 distally. Sampled axon counts were significantly higher than full manual, especially distally (sampled manual: 15,316 ± 4,613, P < 0.001; sampled automated: 16,297 ± 7,733, P = 0.037). All three methods showed strong, significant correlation with each other, especially for distal sections (full manual and sampled manual: \( r_s = 0.912, P < 0.001 \); full manual and sampled automated: \( r_s = 0.599, P = 0.002 \); sampled manual and sampled automated: \( r_s = 0.708, P < 0.001 \)). Overall full manual fiber diameter, axon diameter, and myelin sheath thickness were 5.42 ± 1.18 µm, 3.61 ± 0.78 µm, and 0.93 ± 0.28 µm, respectively. They did not differ from sampled measurements (\( P = 0.144, P = 0.059, \) and \( P = 0.817, \) respectively).

CONCLUSIONS: Manual count of sampled nerve sections produces highly correlated, reliable results when using standardized and systematic sampling methods. Automated data should be regarded with more caution as correlation was not as high. However, the significant correlation indicates it is an acceptable technique if manual sampled analysis is not possible. Although the methods explored in this study correlated highly with one another, the accuracy of both sampled techniques differed significantly from full manual analysis. Therefore, comparison of numerical results between papers reporting these parameters (ie, for a metanalysis) may not be possible. Researchers must be cognizant of the wide variety of techniques reported in the literature and exercise caution when comparing data between studies.

The Relationship of Psychiatric Variables in Patients Undergoing Peripheral Nerve Surgery for Migraine Headache

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BACKGROUND: Patients seeking peripheral nerve surgery for their headaches often have debilitating symptoms that can affect both their functional and psychological well-being. Although prior studies have shown strong associations between psychiatric variables and migraine headaches, their associations in patients undergoing peripheral nerve surgery have not been fully elucidated. This study aims to explore the relationship of psychiatric comorbidities in patients undergoing peripheral nerve surgery for their headaches.

METHODS: One hundred twenty-nine patients were enrolled prospectively and completed the Patient Health Questionnaire-2 (PHQ-2) and Migraine Headache Index (MHI) surveys preoperatively and at 12 months postoperatively. Data on psychiatric comorbidities were collected both via survey and via retrospective chart review.

RESULTS: Preoperatively, 38% of patients self-reported a diagnosis of depression, whereas 45% of patients met PHQ2 criteria for likely major depressive disorder (PHQ-2 score of 3 or greater). Twenty-seven percent of patients reported a diagnosis of generalized anxiety disorder. Patients with depressive symptoms and self-reported anxiety were more likely to report a higher severity of migraine symptoms. At 1-year postoperatively, patients reported a significant decrease in their PHQ-2 score (\( P = 0.02 \)), with 22% of patients reporting depressive symptoms, as compared to 45% preoperatively. The preoperative presence of anxiety or depression did not affect postoperative outcomes.

CONCLUSION: There is a high prevalence of psychiatric ailment in patients undergoing migraine surgery. Comorbid psychiatric conditions do not appear to affect postsurgical outcomes. However, surgery is associated with a significant decrease in depressive symptoms. Prior studies have shown that the surgical treatment of migraine headaches is associated with improved headache symptoms and functionality. This study demonstrates that surgery is also associated with improved psychiatric symptoms.

Clinical Effectiveness of Peripheral Nerve Blocks for Diagnosis of Migraine Trigger Points

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