Original Article
Iranian Journal of Otorhinolaryngology, Vol.38(5), Serial No.148, Sep-2026

Potential Histological Benefits of Gabapentin in Experimental Facial Nerve Crush Injury in Rats: Increased Myelinated Axons and S100-Positive Schwann Cells

Farzaneh Fagheei[1], Maliheh Jahromi[2], *Mohammad Javad Saeedi-Borujeni[3,4]

Abstract

Introduction:

Some studies have shown that gabapentin administration is associated with neuroregeneration. The current study aimed to investigate the effects of daily gabapentin administration on the histological alterations of the facial nerve (FN) following experimental crush injury in Wistar rats.

Materials and Methods:

Twenty-one Wistar rats were randomly divided into three groups of seven: a sham-control group, a vehicle group, and a gabapentin group that received gabapentin after nerve injury induction. At the end of the intervention, the animals were sacrificed under anesthesia, and FN tissue samples were collected to evaluate the number of myelinated axons and Schwann cells. The data were analyzed using SPSS software, and a *P* value of less than 0.05 was considered statistically significant.

Results:

The mean number of myelinated axons was 37.00 ± 2.65 in the sham-control group, 19.86 ± 2.85 in the vehicle group, and 27.29 ± 2.93 in the gabapentin group, with the latter showing an intermediate value between the other two groups ($\eta^2 = 0.879$; $P < 0.001$). Similarly, the highest mean Schwann cell count was observed in the sham-control group (43.00 ± 2.89), whereas the lowest was found in the vehicle group (21.72 ± 2.06). The mean Schwann cell count in the gabapentin group was 34.29 ± 2.87 ($\eta^2 = 0.928$; $P < 0.001$).

Conclusion:

Daily gabapentin administration following FN crush injury resulted in a considerable increase in myelinated axons and S100-positive Schwann cells. These findings suggest that gabapentin may support structural nerve repair after FN injury. Further functional evaluation and cellular and molecular studies are needed.

Keywords: Gabapentin; Facial Nerve; Neuroregeneration

Received date: 25 Jun 2026
Accepted date: 29 Jul 2026

**Please cite this article;* *Fagheei F, Jahromi M, Saeedi-Borujeni MJ. Potential Histological Benefits of Gabapentin in Experimental Facial Nerve Crush Injury in Rats: Increased Myelinated Axons and S100-Positive Schwann Cells Iran J Otorhinolaryngol. 2026:38(5):317-325. Doi:10.22038/ijorl.2026.96859.4182*

[1]*School of Dentistry, Student Research Committee, Isf.C, Islamic Azad University, Isfahan, Iran.*
[2]*Clinical Development Research Center, Na.C, Islamic Azad University, Najafabad, Iran.*
[3]*Department of Medical Basic Sciences, School of Dentistry, Isf.C, Islamic Azad University, Isfahan, Iran.*
[4]*Community Health Research Center, Isf.C, Islamic Azad University, Isfahan, Iran.*
***Corresponding author:** E-mail: j.saeedi@iau.ac.ir*

Introduction

Unwanted facial nerve (FN) injury remains a significant concern in ear, nose, and throat (ENT) and head and neck surgery (1). The FN can be compromised by temporal bone fractures, parotid gland surgery, malignancies, or other iatrogenic causes, resulting in facial asymmetry, dysphagia, impaired eyelid movement, and considerable psychosocial distress (2,3). Although peripheral nerves possess a certain capacity for regeneration, FN repair remains challenging due to its complex sensory, motor, and parasympathetic components and may result in persistent functional deficits, synkinesis, or muscle atrophy (3,4). Therefore, the development of therapeutic strategies aimed at enhancing nerve regeneration and improving functional recovery remains an important area of investigation. Among the various experimental models used to simulate FN injury, nerve crush injury closely resembles clinical conditions because it induces axonal damage while preserving the continuity of the nerve structure (5). Following crush injury, a well-coordinated regenerative process is initiated, involving Wallerian degeneration, clearance of cellular debris by macrophages, activation of Schwann cells, and subsequent axonal regeneration from the proximal to the distal segment (6). Schwann cells play a pivotal role in peripheral nerve regeneration by secreting neurotrophic factors and providing structural guidance for axonal regrowth (7).

Gabapentin (GBP), a structural analogue of γ-aminobutyric acid (GABA), is commonly prescribed for the management of neuropathic pain and neurological disorders such as epilepsy (8). Pharmacologically, GBP binds to the α2δ subunit of voltage-gated calcium channels, thereby modulating calcium influx and neurotransmitter release (9,10). In recent years, accumulating evidence has suggested that the biological effects of GBP may extend beyond its analgesic properties. GBP has been proposed to exert neuroprotective and regenerative effects through several molecular mechanisms, including attenuation of neuroinflammation, reduction of excitotoxic stress, modulation of neuronal plasticity, and improvement of the regenerative microenvironment following nerve injury (11,12). Previous studies have demonstrated that GBP administration may contribute to functional and structural recovery in injured peripheral nerves, including the median and sciatic nerves (13). These findings suggest that GBP may influence molecular pathways involved in peripheral nerve regeneration. However, regeneration following injury to sensory or mixed peripheral nerves, such as the median and sciatic nerves may differ from the repair process of the FN, which contains sensory, motor, and parasympathetic fibers. Therefore, the present study aimed to investigate the effects of daily GBP administration on histological changes in the FN following experimental crush injury in Wistar rats.

Materials and Methods

Animals and study groups

A total of 21 male Wistar rats (6–8 weeks old, weighing 250–300 g) were included in this study. The rats were obtained from the Royan Institute (Isfahan, Iran) and transferred to the animal facility of Islamic Azad University, Najafabad Branch. All animals were handled and cared for humanely in accordance with the criteria outlined in the Guide for the Care and Use of Laboratory Animals published by the Iran National Committee for Ethics in Biomedical Research. The study protocol was approved by the Ethics Committee of Islamic Azad University, Isfahan (Khorasgan) Branch (KHUISF) (IR.IAU.KHUISF.REC.1404.611). The animals were randomly assigned to three groups (n = 7 per group): (1) the sham-control group, in which all surgical procedures were performed without inducing nerve crush injury; (2) the vehicle group, in which animals underwent the same surgical procedures and FN crush injury and subsequently received oral gavage administration of the GBP vehicle (isotonic sterile saline) for 30 days; and (3) the GBP group, in which animals received GBP (Lupin Limited, India) at a dose of 300 mg/kg by oral gavage for 30 days following FN crush injury. The selected GBP dose was based on previous studies (14).

Surgical procedures

Animals were anesthetized under sterile conditions using ketamine (100 mg/kg) and xylazine (10 mg/kg). The left facial region of each rat was shaved, and a horizontal skin incision was made in the subauricular area

extending toward the mandibular region. The skin and subcutaneous tissues were carefully retracted to expose the parotid gland, which was subsequently removed to facilitate visualization of the FN. The main trunk of the FN was identified and exposed anterior to the posterior belly of the digastric muscle. A standardized crush injury was induced approximately 1 cm proximal to the trifurcation point of the FN using a vascular clamp applied for 30 seconds.

Following nerve injury, the muscle and skin layers were closed using 4-0 Vicryl and nylon sutures, respectively (Figure 1). After completion of the surgical procedure, oxytetracycline spray was applied to the incision site to reduce the risk of postoperative infection.

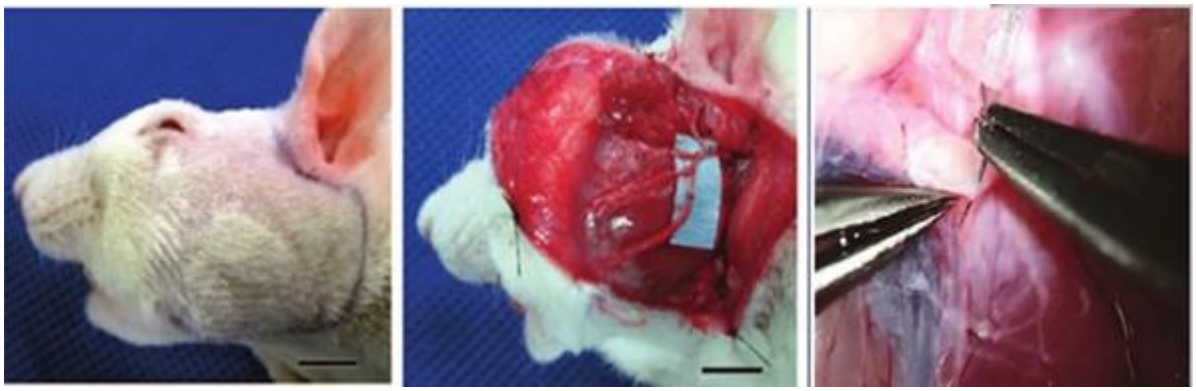

Fig 1. Surgical procedure for inducing FN injury in rats

Histological Examination

Eight weeks after surgery, the animals were anesthetized using the same protocol, and the FN was re-exposed through the previously described surgical approach. The FN samples were collected and immediately placed in wide-mouth containers containing 10% formalin. The samples were fixed in formalin for 36 hours, and the fixative solution was replaced daily to ensure adequate tissue penetration and optimal fixation. Following fixation, the required reagents for the Autotechnicon tissue processor were prepared, and the samples were placed in porous cassettes and processed using the device according to standard tissue-processing protocols. After completion of tissue processing, the samples underwent paraffin embedding.

Briefly, paraffin wax was heated to approximately 56°C, and L-shaped metal molds were prepared. Each tissue sample was positioned in the center of the mold, embedded in molten paraffin, and allowed to cool. After solidification, the paraffin blocks were removed from the molds and stored at 4°C until sectioning. Tissue sections were prepared using a microtome at a thickness of 5 µm. The sections were stained with toluidine blue for visualization of myelin sheaths and examined under a light microscope. To quantify the mean number of myelinated axons, nine images were randomly captured from comparable regions of the FN at ×400 magnification under identical imaging conditions for each group. Five randomly selected fields from each image were analyzed using ImageJ software (Version 1.53, National Institutes of Health, Bethesda, MD, USA), and the mean number of myelinated nerve fibers was calculated.

To minimize observer bias, all image analyses were performed by an investigator blinded to group allocation. Quantitative measurements were independently repeated, and the average values were used for statistical analysis to ensure consistency and reproducibility of the results.

Immunohistochemistry staining

In this study, immunohistochemical (IHC) staining was performed to identify Schwann cells using S100 as a specific cellular marker. For S100 immunostaining, paraffin-embedded tissue sections were first deparaffinized by immersion in xylene for 10 minutes followed by rehydration through a graded ethanol series (100%, 96%, 90%, and 70%) for 3 minutes at each concentration. The sections were

subsequently rinsed with distilled water for 3 minutes. Antigen retrieval was performed by placing the slides in Tris-EDTA buffer and heating them in a microwave oven for 15 minutes. After cooling at room temperature in distilled water for 15 minutes, the sections were washed with phosphate-buffered saline (PBS) for 10 minutes. To block nonspecific antibody binding, the sections were incubated with 5% normal goat serum at 37°C for 1 hour. Subsequently, the sections were incubated with the primary anti-S100 antibody overnight at 37°C. After washing with PBS, the sections were incubated with the appropriate secondary antibody at 37°C for 1 hour.

The slides were then washed with PBS (10 times) and incubated with 3, 3′-diaminobenzidine (DAB) chromogen solution for 4 minutes at room temperature. Following a final PBS rinse (3–4 dips), the sections were dehydrated and mounted with coverslips. The stained sections were examined using a light microscope (Olympus BX51, Japan). For each section, five images were randomly captured at ×100 magnification using a digital camera under identical imaging conditions. The intensity of S100 immunoreactivity was quantified using ImageJ software by measuring the positively stained area. All quantitative analyses were performed by an investigator blinded to group allocation to minimize observer bias.

Measurements were independently repeated to confirm the reliability of the findings, and the mean values were used for statistical analysis.

Statistical analysis

Quantitative data obtained from the histological and immunohistochemical analyses were initially measured using ImageJ software. Statistical comparisons among the experimental groups were performed using one-way analysis of variance (ANOVA), followed by Tukey's post hoc test. Statistical analyses were conducted using SPSS software version 28.0 (SPSS Inc., Chicago, IL, USA). A p-value of <0.05 was considered statistically significant.

Results

Based on the findings, the highest mean number of myelinated axons was observed in the sham-control group (37.00 ± 2.65), whereas the lowest mean number was observed in the vehicle group (19.86 ± 2.85). The GBP group showed an intermediate mean number of myelinated axons (27.29 ± 2.93) compared with the other two groups. These findings indicate that FN crush injury significantly reduced the number of myelinated axons compared with the sham-control group, whereas GBP administration increased the mean number of myelinated axons compared with the vehicle group. The distribution of axon counts across the experimental groups is presented in Figure 2. To evaluate differences in the number of myelinated axons among the experimental groups, one-way analysis of variance (ANOVA) was performed, followed by Tukey's post hoc test for pairwise comparisons when significant differences were detected. The ANOVA results demonstrated a statistically significant difference in the mean number of myelinated axons among the three experimental groups ($\eta^2 = 0.879$; $P < 0.001$).

The calculated effect size ($\eta^2 = 0.879$) indicates that approximately 87.9% of the variability in axon counts was explained by the experimental intervention, while the remaining variance was attributable to other factors and random error. According to Cohen's criteria, a η^2 value ≥ 0.14 represents a large effect size. Therefore, the observed effect size indicates a very strong association between the intervention and axonal regeneration, suggesting that GBP administration had a substantial impact on the number of myelinated facial nerve axons with considerable practical significance.

Based on the immunohistochemical evaluations, the highest mean number of S100-positive Schwann cells was observed in the sham-control group (43.00 ± 2.89), whereas the lowest value was observed in the vehicle group (21.72 ± 2.06).

The GBP group showed an intermediate mean number of S100-positive Schwann cells (34.29 ± 2.87) compared with the other two groups. These findings indicate that FN crush injury significantly reduced the number of S100-positive Schwann cells compared with the sham-control group, whereas GBP administration increased the mean number of S100-positive Schwann cells compared with the vehicle group.

The distribution of Schwann cell counts across the experimental groups is presented in Figure

3. One-way analysis of variance (ANOVA) revealed a statistically significant difference in the mean number of S100-positive Schwann cells among the three experimental groups ($\eta^2 = 0.928$; $P < 0.001$).

The calculated effect size ($\eta^2 = 0.928$) indicates that approximately 92.8% of the variability in S100-positive Schwann cell counts was explained by the experimental intervention, while the remaining variability may be attributed to other factors and random error. According to Cohen's criteria, a η^2 value ≥ 0.14 represents a large effect size.

Therefore, the observed η^2 value indicates a very strong effect of the intervention on S100-positive Schwann cell counts, suggesting that GBP administration was associated with substantial changes in this histological marker.

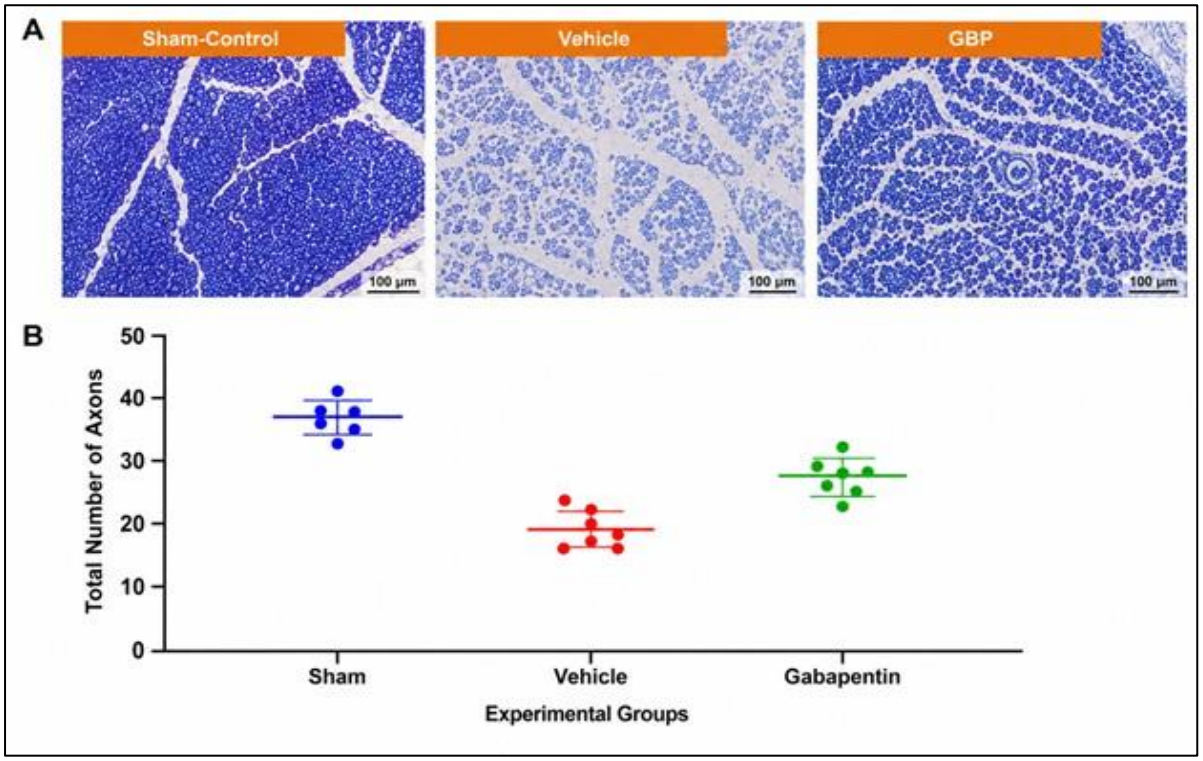

Fig.2. (A) Toluidine blue staining in different groups .(B) Distribution of axon numbers in three experimental groups.Each point represents the number of axons in one sample. The horizontal line represents the mean of each group and the vertical lines represent the standard deviation.

To evaluate the adequacy of the sample size and the ability of the study design to detect the true effects of the intervention, a post hoc power analysis was performed using G*Power software (Version 3.1.9.7; Heinrich Heine University Düsseldorf, Düsseldorf, Germany). Statistical power ($1-\beta$) represents the probability of correctly rejecting the null hypothesis, and values greater than 0.80 are generally considered acceptable for ensuring adequate statistical power. The analysis was conducted using a one-way ANOVA model with three groups, a total sample size of 21 animals, and a significance level of $\alpha = 0.05$. The effect size obtained from the one-way ANOVA results was expressed as eta squared (η^2) and subsequently converted to Cohen's f using the following equation:

$f = \sqrt{(\eta^2 / (1 - \eta^2))}$

Based on this conversion, the effect size for the number of myelinated axons ($\eta^2 = 0.879$) was calculated as $f = 2.695$, while the effect size for S100-positive Schwann cell counts ($\eta^2 = 0.928$) was calculated as $f = 3.590$. The estimated statistical power exceeded 0.99 for both outcome variables. Therefore, considering that the calculated statistical power was substantially higher than the commonly accepted threshold of 0.80, the sample size used in this study was considered sufficient to detect the observed differences among groups. These findings indicate a low probability of type II error and support the reliability of the statistical comparisons performed.

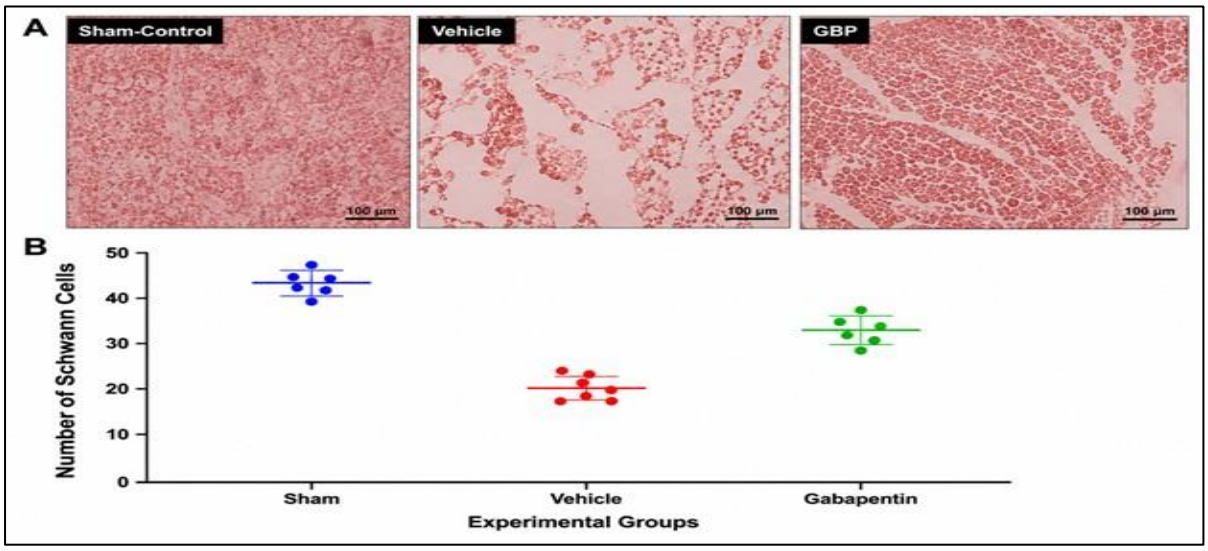

Fig. 3. (A) Immunohistochemical staining of S100. (B) Distribution of Schwann cell numbers in three experimental groups. Each point represents the number of axons in one sample. The horizontal line represents the mean of each group and the vertical lines represent the standard deviation.

Discussion

In the present study, the effect of GBP administration on histological changes following FN crush injury in Wistar rats was investigated. GBP is an anticonvulsant medication primarily used for the treatment of partial seizures and neuropathic pain (15). It is considered a first-line therapeutic option for several neuropathic pain conditions, including diabetic neuropathy, post-herpetic neuralgia, and central neuropathic pain (16,17).

In recent years, increasing attention has been directed toward the potential neuroprotective and regenerative properties of GBP beyond its established analgesic effects. In our study, GBP administration resulted in significant structural improvements following FN crush injury compared with the vehicle group. The main finding of the present study was that daily administration of GBP for one month after FN injury was associated with increased numbers of myelinated axons and S100-positive Schwann cells compared with untreated animals. These findings suggest that GBP may positively influence structural aspects of peripheral nerve repair and indicate a potential role for this widely available medication as an adjunctive approach in FN injury recovery. One of the major findings of this study was the increased number of myelinated axons in the GBP-treated group compared with the vehicle group. Myelinated axons are essential components of effective nerve conduction and functional recovery (18). Therefore, the increased number of myelinated axons observed following GBP administration may reflect a favorable influence on the regenerative environment after FN injury. Additionally, the increased presence of S100-positive Schwann cells in the GBP group provides further evidence of potential modulation of the cellular processes involved in nerve repair. Schwann cells play a central role in peripheral nerve regeneration by supporting axonal growth, secreting neurotrophic factors, and contributing to remyelination (19,20). The simultaneous increase in S100-positive Schwann cells and myelinated axons suggests that GBP may promote a regenerative microenvironment that facilitates axonal restoration and remyelination. However, further cellular and molecular investigations are required to clarify the underlying mechanisms.

Several mechanisms have been proposed to explain the potential neuroregenerative effects of GBP. By binding to the α2δ subunit of voltage-gated calcium channels, GBP reduces calcium influx and modulates neurotransmitter release, potentially limiting excitotoxic processes following nerve injury (21). Previous studies have suggested that GBP may influence signaling pathways involved in axonal growth and regeneration, including the mammalian target of rapamycin (mTOR) pathway (22). In

addition, GBP has been associated with reduced neuroinflammatory responses through modulation of activated glial cells, including microglia and astrocytes (23,24). Another possible mechanism involves the regulation of neurotrophic factors, such as brain-derived neurotrophic factor (BDNF), which plays an important role in neuronal survival, growth, and regeneration (25). Figure 4 summarizes the proposed mechanisms through which GBP may contribute to peripheral nerve regeneration.

Based on our literature review, most previous studies investigating the regenerative effects of GBP have focused on peripheral nerves other than the FN. Machado et al. investigated the effect of GBP on regeneration following experimentally transected median nerve injury in rats (14). Using a functional assessment model based on grasping ability, they demonstrated improved sensory and motor recovery after 30 days of GBP administration. The findings of the present study are consistent with those reported by Machado et al., despite differences in the injured nerve type and experimental model. Similarly, Farzamfar et al. evaluated the effects of GBP supplementation in a sciatic nerve injury model using an in vitro tissue engineering approach (26). Their findings demonstrated that GBP incorporation into nerve-related scaffolds enhanced regenerative responses and supported nerve repair. Consistent with these observations, our study provides histological evidence suggesting that GBP may positively influence the structural regeneration of an injured peripheral nerve, specifically the FN.

An important consideration in translational animal studies is the extent to which the experimental model reflects clinical conditions. In the present study, an FN crush injury model was used because it resembles several clinical scenarios in which axonal disruption occurs while nerve continuity is preserved. GBP administration resulted in increased numbers of myelinated axons and S100-positive Schwann cells, indicating potential beneficial effects on structural processes associated with nerve repair.

Nevertheless, these findings should be interpreted cautiously, as histological improvement does not necessarily represent complete functional recovery. Restoration of FN function depends on multiple factors, including appropriate axonal guidance, accurate target reinnervation, and recovery of neuromuscular activity, none of which were directly evaluated in this study. Several limitations should be acknowledged.

First, the molecular pathways responsible for the potential regenerative effects of GBP were not investigated. Second, S100 immunostaining reflects the presence of Schwann cells but does not directly indicate Schwann cell proliferation; therefore, increased S100 positivity should be interpreted as increased Schwann cell presence rather than definitive cellular proliferation. Third, functional assessments, such as electrophysiological measurements and behavioral evaluations, were not performed.

Finally, because this study was conducted in an animal model, direct extrapolation of these findings to human FN injury recovery requires further investigation. Future studies incorporating functional assessments, molecular analyses, and specific proliferation markers such as Ki-67 may provide deeper insight into the regenerative mechanisms of GBP and determine whether structural improvements translate into meaningful functional recovery.

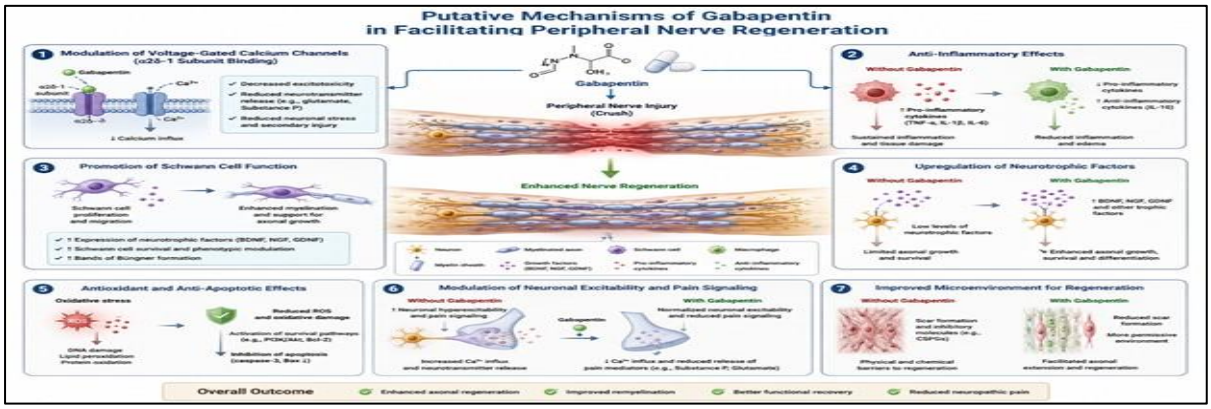

Fig. 4: Some of the proposed mechanisms for the possible role of GBP in peripheral nerve regeneration

Conclusion

In conclusion, daily GBP administration following FN crush injury was associated with a significant increase in the number of myelinated axons and S100-positive Schwann cells. These findings suggest a potential beneficial effect of GBP on structural changes related to peripheral nerve repair. The observed histological improvements indicate that GBP may modulate cellular processes involved in axonal regeneration and remyelination following nerve injury.

Considering the clinical significance of FN dysfunction and the limited availability of effective pharmacological therapies, the present findings provide preliminary experimental evidence supporting further investigation of GBP as a potential adjunctive treatment strategy for FN injury. Future studies focusing on the underlying cellular and molecular mechanisms, as well as functional outcomes, are warranted to better define the therapeutic potential of GBP in facilitating FN recovery.

Acknowledgements

Our study was supported by KHUISF Deputy Research. We gratefully thank the Vice Chancellor for research, KHUISF. Artificial intelligence (ChatGPT, OpenAI) was used solely for the preparation of the graphical illustration shown in Figure 4. All scientific concepts, interpretation of findings, and final figure content were reviewed and approved by the authors.

References

1. Zamzam SM, Hassouna MS, Elsawy MK, Gafaar SH. Otolaryngologists and iatrogenic facial nerve injury: a meta-analysis. Egypt J Otolaryngol. 2023; 39(1):71.

2. Moncaliano MC, Ding P, Goshe JM, Genther DJ, Ciolek PJ, Byrne PJ. Clinical features, evaluation, and management of ophthalmic complications of facial paralysis: A review. J Plast Reconstr Aesthet Surg. 2023;87:361-368.

3. Maxwell AK, Lemoine JC, Kahane JB, Gary CC. Management of the facial nerve following temporal bone ballistic injury. Laryngoscope Investig Otolaryngol. 2022;7(5):1541-1548.

4. Kim J. Prevention and treatment of post-paralytic synkinesis: critical changes following severe facial palsy. J Electrodiagn Neuromuscul Dis. 2024;26(2):19-24. doi:10.18214/jend. 2024. 00038.

5. Fei J, Guan X, Gao L, Ni P, Zheng H, Duan K, et al. Establishment of a facial nerve trunk crush injury model and evaluation of facial nerve self-healing in rats. Brain Behav. 2023;13(9):e3156.

6. Ye Z, Wei J, Zhan C, Hou J. Role of transforming growth factor beta in peripheral nerve regeneration: cellular and molecular mechanisms. Front Neurosci. 2022;16:917587.

7. Xu H, Fan Z. The role and mechanism of Schwann cells in the repair of peripheral nerve injury. Cell Tissue Res. 2025;400(1):81-95.

8. Tony RM, El Hamd MA, Gamal M, Saleh SF, Maslamani N, Alsaggaf WT, et al. Green bio-analytical study of gabapentin in human plasma coupled with pharmacokinetic and bioequivalence assessment using UPLC-MS/MS. Separations. 2023;10(4):234.

9. Chen Z, Mondal A, Minor DL Jr. Structural basis for CaVα2δ: gabapentin binding. Nat Struct Mol Biol. 2023;30(6):735-739.

10. Huang Y, Chen SR, Pan HL. α2δ-1-linked NMDA and AMPA receptors in neuropathic pain and gabapentinoid action. J Neurochem. 2025; 169(4): e70064.

11. Kucun N, Ates I, Lalogu E, Ozmen S, Yildirim S, Pur B, et al. Pregabalin and gabapentin's roles in nerve regeneration: multifaceted analysis in an experimental model. Turk Neurosurg. 2025; 35(6):880-890. doi:10.5137/1019-5149.JTN.47696-24.2.

12. Ozbek Z, Aydin HE, Kocman AE, Ozkara E, Sahin E, Bektur NE, et al. Neuroprotective effect of genistein in peripheral nerve injury. Turk Neurosurg. 2017;27(5):816-822. doi:10.5137/1019-5149.JTN.18549-16.1.

13. Canpolat M, Çolpak HA, Günay Canpolat D, Önder GÖ, Yetkin MF, Yay AH, et al. Comparison of the effectiveness of rapamycin and gabapentin treatment in rats with induced sciatic nerve injury. Erciyes Med J. 2022;44(1):56-62. doi: 10.14744/ etd.2021.87405.

14. Machado J, Ghizoni M, Bertelli J, Teske GC, Teske GC, Martins D, et al. Stretch-induced nerve injury: a proposed technique for the study of nerve regeneration and evaluation of the influence of gabapentin on this model. Braz J Med Biol Res. 2013; 46(11):929-935.

15. Sharma H, Kannaiah KP, Obaydo RH, Keshishian R, Chanduluru HK, Bhattarai K, et al. Green analytical chemistry in gabapentin analysis: methods and sustainability review. Talanta Open. 2025; 11:100465.

16. Mauermann ML, Staff NP. Peripheral neuropathy: a review. JAMA. 2026;335(3):255-266. doi:10.1001/jama.2025.19400.

17. Attar AA, Halabi MH, Barnawi ET, Sindi GK, Altayeb AA, Fadel FT, et al. Evaluating the efficacy

and safety of duloxetine and gabapentin in managing diabetic neuropathy: a systematic review and meta-analysis. Br J Pain. 2025;19(5):358-370.

18. Verardo C, Romeni S, Micera S. Biophysical characterization of the recording of unmyelinated and myelinated fiber activity with peripheral interfaces. iScience. 2025;28(5):112495. doi:10.1016/j.isci.2025.112495.

19. Shurin MR, Wheeler SE, Zhong H, Zhou Y. Pathologic and therapeutic Schwann cells. Cells. 2025;14(17):1336.

20. Follis R, Prabhu VV, Carter BD. The influence of Schwann cell metabolism and dysfunction on axon maintenance. Glia. 2025;73(12):2338-2352.

21. Reyes Fernandez PC, Wright CS, Warden SJ, Hum J, Farach-Carson MC, Thompson WR. Effects of gabapentin and pregabalin on calcium homeostasis: implications for physical rehabilitation of musculoskeletal tissues. Curr Osteoporos Rep. 2022;20(6):365-378.

22. Yan BC, Wang J, Rui Y, Cao J, Xu P, Jiang D, et al. Neuroprotective effects of gabapentin against cerebral ischemia reperfusion-induced neuronal autophagic injury via regulation of the PI3K/Akt/mTOR signaling pathways. J Neuropathol Exp Neurol. 2019;78(2):157-171.

23. Zhang Z, Jiang J, He Y, Cai J, Xie J, Wu M, et al. Pregabalin mitigates microglial activation and neuronal injury by inhibiting HMGB1 signaling pathway in radiation-induced brain injury. J Neuroinflammation. 2022;19(1):231.

24. Gu D, Xia Y, Ding Z, Qian J, Gu X, Bai H, et al. Inflammation in the peripheral nervous system after injury. Biomedicines. 2024;12(6):1256.

25. Vanelderen P, Rouwette T, Kozicz T, Heylen R, Zundert JV, Roubos EW, et al. Effects of chronic administration of amitriptyline, gabapentin and minocycline on spinal brain-derived neurotrophic factor expression and neuropathic pain behavior in a rat chronic constriction injury model. Reg Anesth Pain Med. 2013;38(2):124-130.

26. Farzamfar S, Naseri-Nosar M, Vaez A, Esmaeilpour F, Ehterami A, Sahrapeyma H, et al. Neural tissue regeneration by a gabapentin-loaded cellulose acetate/gelatin wet-electrospun scaffold. Cellulose. 2018;25(2):1229-1238.