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Influences of Glabridin Treatment on Motor Function Recovery after Spinal Cord Injury

Influencia del Tratamiento con Glabridina en la Recuperación de la Función Motora después de una Lesión de la Médula Espinal

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SUMMARY: Spinal cord injury (SCI) usually arises from compression due to traffic accidents and falls, resulting in varying degrees of movement, sensory loss, and possible paralysis. Glabridin (Gla) is a natural compound derived from licorice. It significantly affects drug development and medicine because of its anti-inflammatory, anti-oxidative, anti-tumoral, antibacterial, bone protective, cardiovascular protective, neuroprotective, liver protective, anti-obesity, and anti-diabetic properties. Various methods were employed to administer Gla to SCI mice in order to investigate its impact on the recovery of motor function. The mice were allocated into four cohorts using a randomization procedure. In the sham cohort, solely the lamina of vertebral arch was surgically exposed without causing any harm to the spinal cord tissue. Conversely, the injury cohort was subjected to spinal cord tissue damage and received no treatment thereafter. The mice in the remaining two cohorts received a dosage of 40 mg/kg Gla every two days via either intraperitoneal or intrathecal injection for a duration of 42 d following spinal cord injury. We conducted behavioral tests utilizing the Basso Mouse Scale score and gait analysis techniques. Magnetic resonance imaging and hematoxylin and eosin were employed to evaluate scar tissue formation. Systemic inflammation in mice was evaluated by employing an enzyme-linked immunosorbent assay. Gla promoted motor function recovery in mice following SCI and improved the pathological environment in the damaged area. These alterations were more evident in mice subjected to the intrathecal injection method. Intraperitoneal injections appear to be more beneficial for controlling systemic inflammatory responses. Although more intensive studies are required, Gla exhibits promising clinical potential as a cost-effective dietary phytochemical.

KEY WORDS: Glabridin; Motor Function; Spinal Cord Injury; Neuroprotection.

ABBREVIATION LIST. SCI: Spinal cord injury, Gla: Glabridin, AD: Alzheimer's disease, IL: Interleukin, TNF: Tumor necrosis factor, BMS: Basso mouse scale, MRI: Magnetic resonance imaging, H&E: Hematoxylin and Eosin, LFB: Luxol Fast Blue, PBS: phosphate-buffered saline, GFAP: glial fibrillary acidic protein, Tuj1: neuronal class III β-tubulin, 5-HT: 5-hydroxytryptamine, ELISA: Enzyme-linked immunosorbent assay, LPS: Lipopolysaccharide

INTRODUCTION

Spinal cord injury (SCI) involves various types; depending on the severity, a wide variety of symptoms occur, ranging from pain to complete impairment of both motor and sensory functions. For millions of people worldwide, SCI often affects the quality of life. However, there is currently no effective treatment (Friedli *et al*., 2015).

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Therefore, the significance of identifying new treatments for patients with SCI is evident. Further exploring its pathogenesis and finding effective treatment strategies are great challenges for researchers.

Glabridin (Gla) is an isoflavone extracted from the roots and rhizomes of Glycyrrhiza glabra L (Simmler *et al*., 2013). Studies of Gla have increased since it was first isolated and identified from roots in 1976 by Saitoh *et al*. (1976). Several investigations have revealed that photolicorice has several biological activities, encompassing whitening, anti-inflammatory, antioxidant, and phytoestrogenic activities (Saitoh *et al*., 1976; Fiore *et al*., 2005).

Inflammation is important in several neurological disorders, encompassing Parkinson's disease, Alzheimer's disease (AD), and multiple sclerosis. Gla has been shown to reduce the generation of interleukin (IL)-1β, tumor necrosis factor (TNF)-α, and NO by downregulating the activity of NF-kB signaling and AP-1 thereby improving memory in AD mice (Park *et al*., 2010). Gla treatment improved memory and reduced brain cholinesterase activity in scopolamine-treated mice. Similarly, 25 mg/kg Gla prevented detrimental damage to learning and memory caused by hyperglycemia (Hasanein, 2011). Gla has been shown to cause sedative and anxiolytic effects by enhancing GABA-mediated responses (Jin *et al*., 2013).

The potential impact of Gla in SCI remains uninvestigated. This study represents the initial investigation into the impact of Gla on motor function recovery following SCI in mice, using different administration methods and validated by multiple methods, encompassing behavioral tests.

MATERIAL AND METHOD

Animals and cell culture. We employed female C57BL/6 mice with an average age of 9 weeks and a mean body weight of 20 g. The mice were housed with a 12:12-h light/dark cycle, and the temperature was maintained at 20-22°C with a relative humidity of 50 %. The present study received approval from the Ethics Committee for Animal Studies at Yangzhou University. Experiments pertaining to animal husbandry and welfare were carried out in accordance with the established protocols of the laboratory at Yangzhou University. The N2A cells used in this study were acquired from ProCell Life Technology Co. Ltd. The cells were cultivated in a modified Eagle medium (Gibco, New York, USA) supplemented with 1 % penicillin/streptomycin and 10 % fetal bovine serum (Gibco, New York, USA). The culture conditions was at 37°C with 5 % CO_2. The fluid is changed every 2 d.

Cell viability. The cytotoxicity of Gla (MedChemExpress, Shanghai, China) (Fig. 1A) was determined employing the Cell Count Kit-8 (MedChemExpress, Shanghai, China). At a density of 10 $\times 10^5$ cells/mL, N2A cells (100 μL) were cultured in 96-well plates for a duration of 24 h, following which they were subjected to various concentrations of Gla (0, 0.01, 0.1, 0.5, 1, 5 mM) for 24 h and 48 h. The absorbance at 450 nm was determined employing the enzyme label one hour after the addition of 10 μL of CCK-8 solution.

Grouping and surgical procedures of the mice. The mice were randomly allocated into four cohorts. Following the administration of 2 % isoflurane anesthesia, the mice underwent a procedure that involved the exposure of the spinal cord at the T10 level. A force of 60 kilodynes was then applied to the spinal cord employing an Infinite Horizon Impactor (W. M. Keck Center for Collaborative Neuroscience, Rutgers State University, New Jersey, USA). A significant hematoma was observed on the surface of the spinal cord contusion (Fig. 2). To mitigate hemorrhaging, a gelatinous sponge of medical origin was positioned at the operative site. Ultimately, the muscles and skin were meticulously stitched together. In the sham cohort, the lamina of vertebral arch was surgically incised to expose the spinal cord without any additional injury.

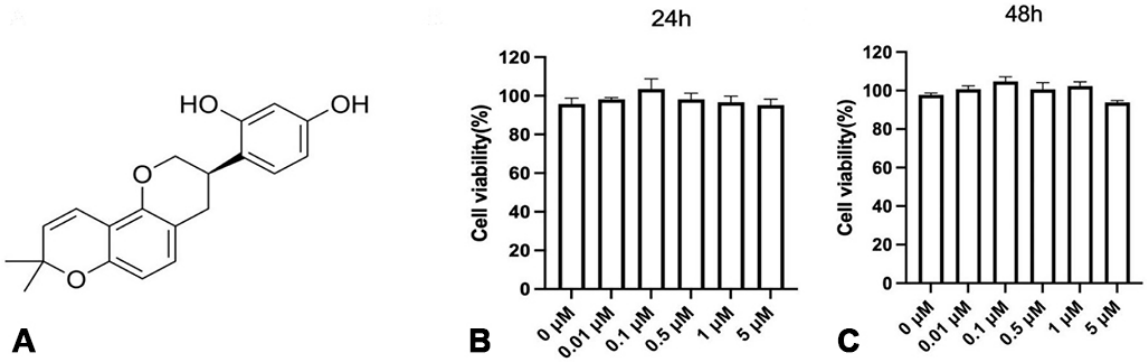

Fig. 1. Effect of Gla on N2A cell viability. A: Chemical structure of Gla. B, C: Cytotoxicity of different Gla concentrations (0, 0.01, 0.1, 0.5, 1, 5 mM) on N2A cells at 24 and 48 h measured using the CCK-8 assay.

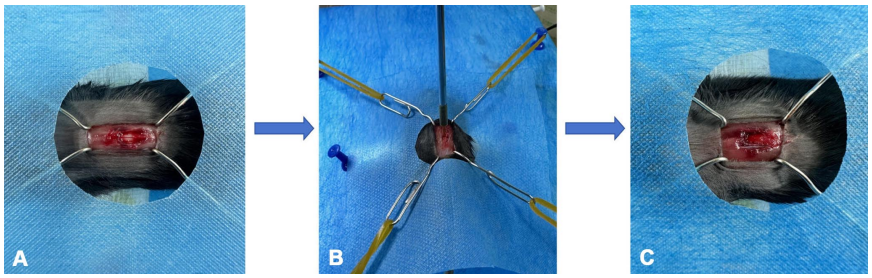

Fig. 2. Surgical procedure of the mice. A: The spinal cord of the mouse is exposed on T10. B: The percussion contuses the spinal cord. C: A significant hematoma appears on the surface of the bruised spinal cord.

Postoperative treatment. The mice were administered ampicillin (150 mg/kg) via intramuscular injection on a daily basis for a duration of seven consecutive days. The bladder underwent manual compression twice a day until voluntary micturition was regained. All mice in the sham or injured cohorts, with the exception of those in the antibiotic cohort, were not subjected to any form of treatment. The injected Gla dose was 10 mg/kg (Dogra *et al*., 2021). One Gla treatment cohort was intraperitoneally injected with 40 mg/kg every 2 d. The other Gla treatment cohort received an intrathecal injection of 40 mg/kg every 2 d.

Assessment of spinal cord functional recovery. The evaluation of hind-limb motor function was conducted by employing the Basso Mouse Scale (BMS) open-field exercise test on specific days following the injury, namely days 1, 3, 5, 7, and 14. Subsequently, the assessment was repeated on a weekly basis for a duration of 6 weeks. The mice's capacity to sustain body posture at progressively escalating angles was evaluated through an oblique task. The animals underwent testing on days 1, 3, 5, 7, and 14 post-injury, followed by weekly assessments for a duration of 6 weeks. At each position, the mice underwent testing, followed by a gradual increase in the angle by 5°. The maximum angle was maintained at a fixed position for 10 s.

A gait analysis was conducted six weeks following SCI. The mice were allowed to crawl on the track of a gait analysis instrument (Xinruan Information Technology Company, Shanghai, China). The measurements comprised step length, which refers to the distance between the centers of consecutive footprints on the same side, and sway distance, which refers to the vertical distance between the centers of the left and right hind limbs. For each condition, an average of three steps was taken into account.

Disease area and demyelination

On day 42, five animals per cohort were subjected to magnetic resonance imaging (MRI). The mice were subjected to anesthesia using flurane at concentrations of 3-4 % for induction and 1.5-2 % for maintenance, administered in a mixture of oxygen (0.4 L/min) and nitrogen (0.6 L/min). The mice were anesthetized and positioned in the prone position on the fiber fixation system. The experiment was conducted employing a small-animal MRI system (Bruker Biospec 11.7T Animal MR scanner; Bruker AXS GmbH, Karlsruhe, Germany). Sequence protocol was conducted with the following parameters: TR: 5000 ms, TE: 25 ms, slice thickness: 0.5 mm, resolution: 0.1 mm × 0.1 mm, average: 2.

The mice received an intraperitoneal injection of 2 % pentobarbital (50 mg/kg) six weeks post-surgery. Following cardiac perfusion with a 4 % paraformaldehyde solution, the spinal cords were promptly dissected and subsequently immersed in a 4 % (w/v) paraformaldehyde solution for an overnight fixation period. The specimens underwent dehydration employing ethanol and were subsequently embedded in paraffin. The tissue embedded in paraffin was sliced into sections that were 4 μm in thickness using a Leica CM 1900 instrument. These sections were subsequently stained using Hematoxylin and Eosin (H&E) and Luxol Fast Blue (LFB) staining.

Immunofluorescence analysis. The specimens underwent sectioning in a cryostat, resulting in horizontal sections with a thickness of 20 μm. The spinal cord sections underwent three washes using 0.01 M phosphate-buffered saline (PBS), followed by incubation with the primary antibody, and were subsequently rinsed three times with PBS. The primary antibodies utilized in this investigation consisted of mouse monoclonal anti-glial fibrillary acidic protein(GFAP) (Diluted at a ratio of 1:200, Sigma, Missouri, USA) for the purpose of labeling astrocytes, mouse monoclonal anti-neuronal class III b-tubulin (Tuj1) antibody (Diluted at a ratio of 1:200, ABclonal, Wuhan, China), and rabbit antibodies targeting rat 5-hydroxytryptamine (5-HT) (Diluted at a ratio of 1:200, ImmunoStar, Wisconsin, USA). Subsequently, the sections were treated with secondary antibodies and subjected to an incubation period of 1 h at room temperature under conditions of darkness. Subsequently, the sections were subjected to a triple wash using PBS and subsequently placed in a light-restricted environment for incubation with DAPI for a duration of 3 min. The surplus DAPI was eliminated through a washing process using PBS. The slides were coated with glycerol and imaged employing a field fluorescence microscope (BX-51; Olympus, Washington, USA) selected at random.

Enzyme-linked immunosorbent assay (ELISA). The concentrations of inflammatory factors in the peripheral blood of the mice were evaluated using ELISA six weeks post-surgery. Following the fixation process, the tails of mice were submerged in water at a temperature of 50°C for a duration of several minutes in order to facilitate the filling of tail vessels. The tail was dried, 1–2 mm tail tips were cut with scissors, and the blood effluent was connected to a test tube. After blood collection, the wound was pressed with a cotton ball to stop the bleeding. The levels of TNF-α and IL-10 in the mouse peripheral blood were measured employing a TNF-α and IL-10 ELISA test kit (BYabscience, Beijing, China), strictly following the manufacturer's instructions.

Statistical analysis. The statistical analysis was conducted utilizing the SPSS software (version 22.0); figures were created using GraphPad Prism 8. Quantitative data are expressed as the mean ± standard deviation, using a t-test with independent samples to compare two cohorts and one-way ANOVA between several cohorts. Statistical significance was set at $P < 0.05$, $P < 0.01$, and $P < 0.001$.

RESULTS

Effect of Gla on the viability of N2A cells. To study the cytotoxic effects of Gla, different concentrations of Gla (0, 0.01, 0.1, 0.5, 1, 5 μM) were added to N2A cells for 24 h and 48 h. The assessment of cell viability was conducted utilizing the CCK-8 assay. As shown in Figures 1B and 1C, Gla had no significant toxic effects on N2A cells.

Gla treatment improves motor performance in mice. The motor function restoration holds significant importance in individuals diagnosed with SCI. The mice in the sham cohort exhibited consistent and enduring footprints six weeks post-surgery. The mice within the injured cohort exhibited impaired toe control during locomotion, resulting in a reduction in stride length and an elevation in swing distance. In comparison to the cohort of individuals who sustained injuries, the Gla-treated cohort exhibited motor function that was more similar to that of the sham cohort. Notably, the administration of Gla via intrathecal injection yielded superior outcomes. The strides in the sham, intraperitoneal, and intrathecal cohorts were 5.16±0.08, 2.62±0.36, and 3.28±0.73 cm, respectively (Figs. 3A and 3B). The sway distance in the intrathecal injection cohort was measured to be 3.68±0.17 cm, a value that was found to be closer to the sway distance observed in the sham cohort (1.82±0.16 cm) (Figs. 3A and 3C).

The evaluation of motor behavior was conducted at regular intervals utilizing the BMS motor score scale. The findings indicated that both the injury cohort and the Gla cohort exhibited significant hind-limb paralysis from days 1 to 7 following the injury. The scores of each cohort

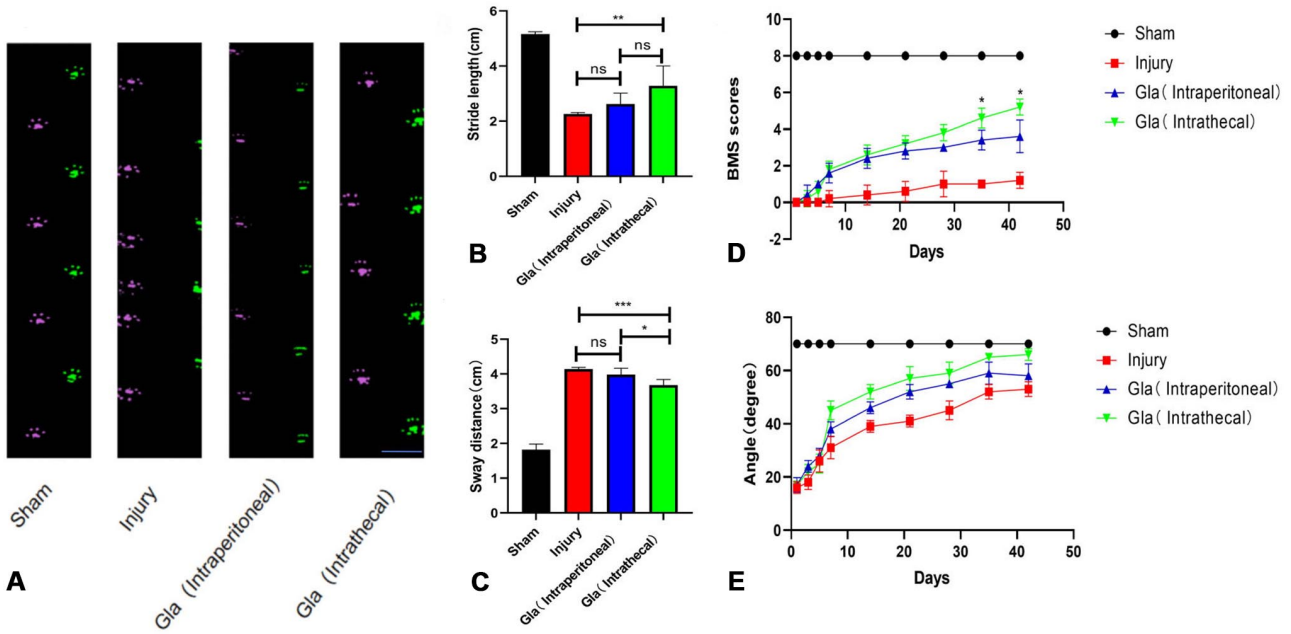

Fig. 3. Assessment of motor function after spinal cord injury (SCI). A: Representative footprint patterns of different groups at 6 weeks after SCI. Scale bar = 1.5 cm. B, C: Semiquantitative analysis of stride length (B) and swing distance (C) in gait analysis. D: Basso Mouse Scale scores of the mice at 6 weeks after SCI. E: Score of tilt plate experiments in mice at 6 weeks after SCI. Data are presented as the mean ± SD (n=5). ***P < 0.001, **P < 0.01, *P < 0.05.

improved over time. After five weeks, the BMS score improved significantly in the Gla treatment cohort; the recovery was greater in the intrathecal injection cohort (4.60±0.48) (Fig. 3D). The difference was not statistically significant in the oblique plate experiment, although the response was greater than that in the injury cohort (Fig. 3E).

Gla treatment enhances the pathological structure and demyelination in the injured area. In order to ascertain the function of Gla in the affected region *in vivo*, we conducted MRI and H&E staining of the site of injury in the thoracic spinal cord of mice, specifically at the T10 level. MRI showed that the lesion area was reduced in the Gla injection cohort contrasted with the injury cohort (Fig. 4A). H&E staining showed that Gla treatment improved the pathological environment in the damaged area (Fig. 4B). A comparable pattern was noted in relation to the protective impacts against myelin. LFB staining exhibits specificity towards myelin, with the blue region indicating positive myelin expression, while the pale region corresponds to areas that have undergone demyelination. The cohort that was injured exhibited demyelinating changes in comparison to the cohort that underwent a sham procedure. Gla treatment protected the myelin tissue compared with the injured cohort (Figs. 4C and 4D).

Gla-treated mice express more immature neurons with less scar tissue formation. The occurrence of a glial scar subsequent to SCI has adverse effects on the process of spinal cord regeneration and repair. To gain a complete understanding of the nerve scar progression, a double staining technique was employed to visualize the expression of GFAP and Tuj1 (Fig. 5A). The expression level of GFAP (4.34±0.21) was observed to be slightly lower in comparison to the injured cohort (4.42±0.24), although the difference was not found to be significant. The intrathecal injection cohort showed lower GFAP levels (3.80±0.33) (Fig. 5B). Tuj1 is also present in immature neuronal cell bodies. As displayed in Figure 6, the intensity of Tuj1 (2.18±0.26) and (3.02±0.40) was greater than that in the injury cohort, and intrathecal injection showed a more pronounced difference than intraperitoneal (Fig. 5C). The 5-HT positive axon intensity represents the recovery of the motor neurons. The results showed that both intraperitoneal injection (3.04±0.15) and intrathecal injection (3.0±0.42) showed significant recovery compared with the injury cohort (Fig. 6).

Gla reduced the inflammatory response in mice with SCI. Previous research has demonstrated that Gla exhibits favorable anti-inflammatory properties. The TNF-α and IL-10 levels were quantified using the ELISA technique in the peripheral serum of SCI mice. As shown in Figure 7, the levels of TNF-α (120.70±2.52) and IL-10 (42.55±3.41) were significantly greater in the injured than in the sham cohort. The Gla treatment cohort showed results opposite to those of the injury cohort. The TNF-a for the intraperitoneal and intrathecal injection cohorts were (64.05±3.46) and (72.44±6.49). The IL-10 levels in the intraperitoneal and intrathecal injection cohorts were (84.47±3.41) and (82.33±2.52).

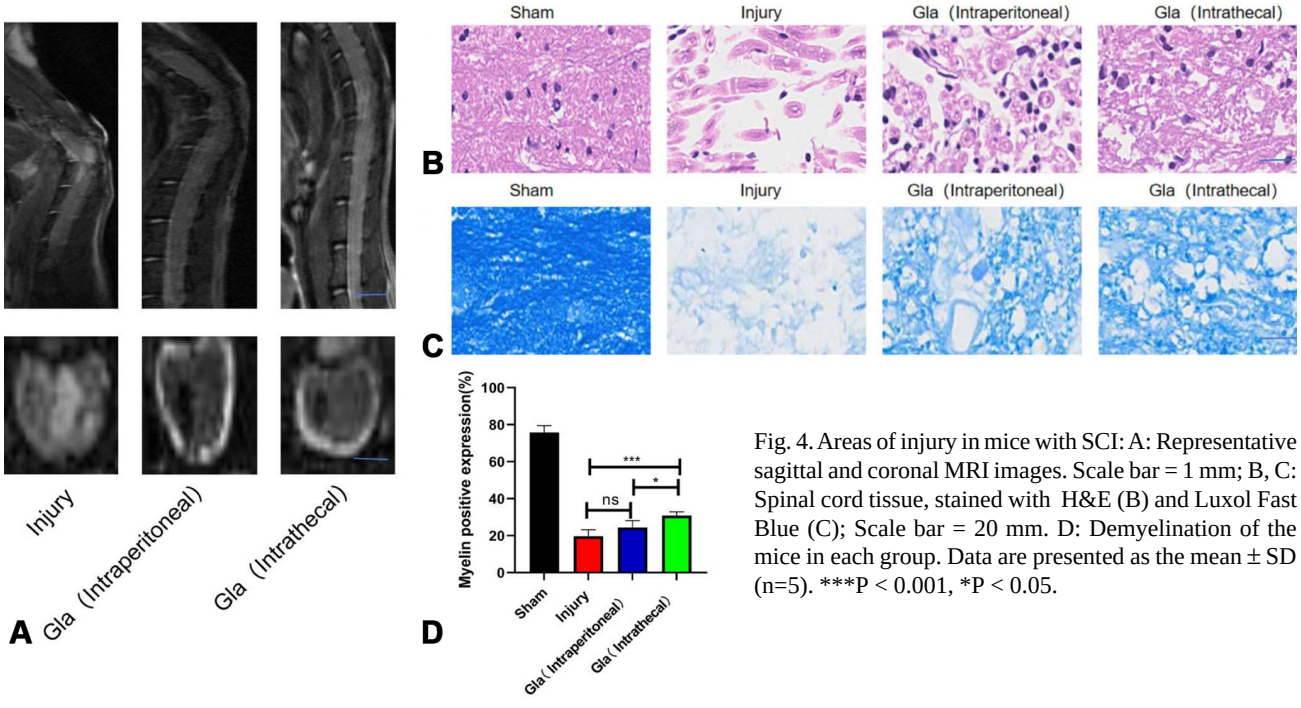

Fig. 4. Areas of injury in mice with SCI: A: Representative sagittal and coronal MRI images. Scale bar = 1 mm; B, C: Spinal cord tissue, stained with H&E (B) and Luxol Fast Blue (C); Scale bar = 20 mm. D: Demyelination of the mice in each group. Data are presented as the mean ± SD (n=5). ***P < 0.001, *P < 0.05.

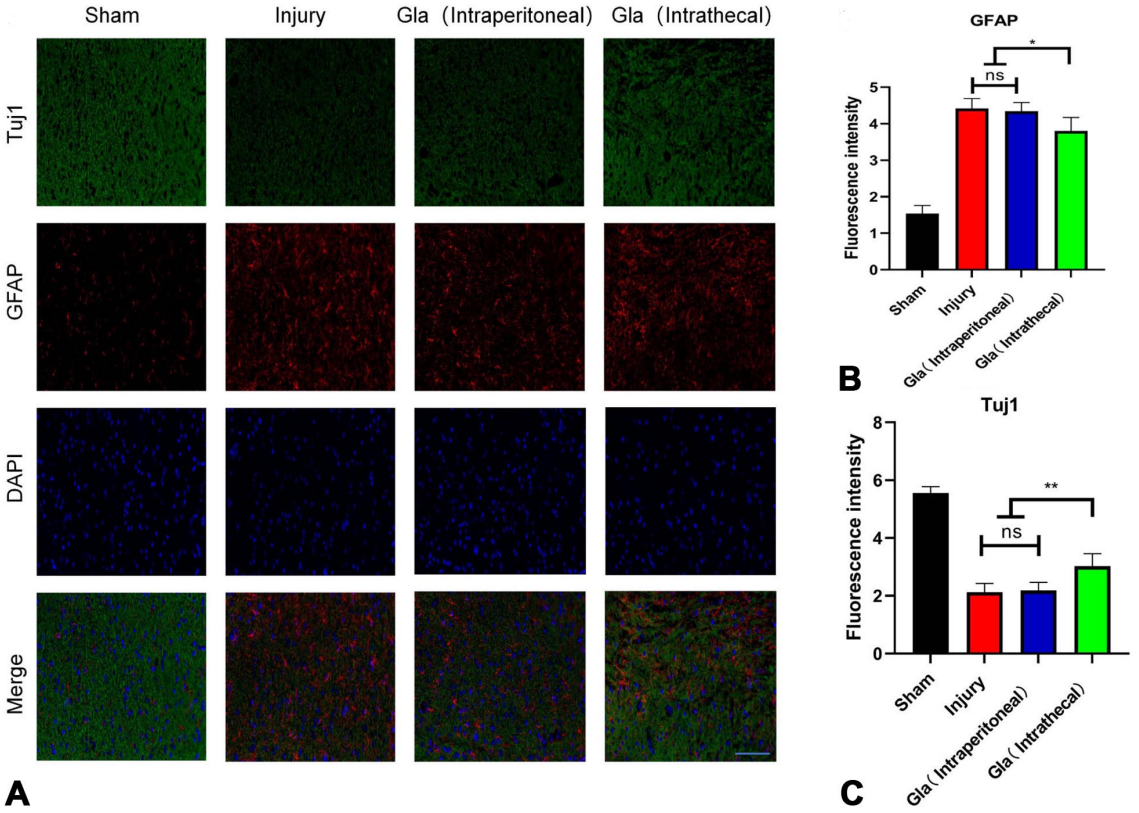

Fig. 5. Glial scar and immature neuron formation in the injured area. A: Analysis of the effects of GFAP (red) and Tuj1 (green) double labeling on glial scar and immature neuron formation after 6 weeks of treatment. Nuclei are stained with DAPI (blue). Scale bar = 50 μm. B, C: GFAP positive cells (B) Tuj1 positive cells (C). The quantitative analysis data of the fluorescence intensity is expressed as the mean ± SD (n=5). **P < 0.01, *P < 0.05.

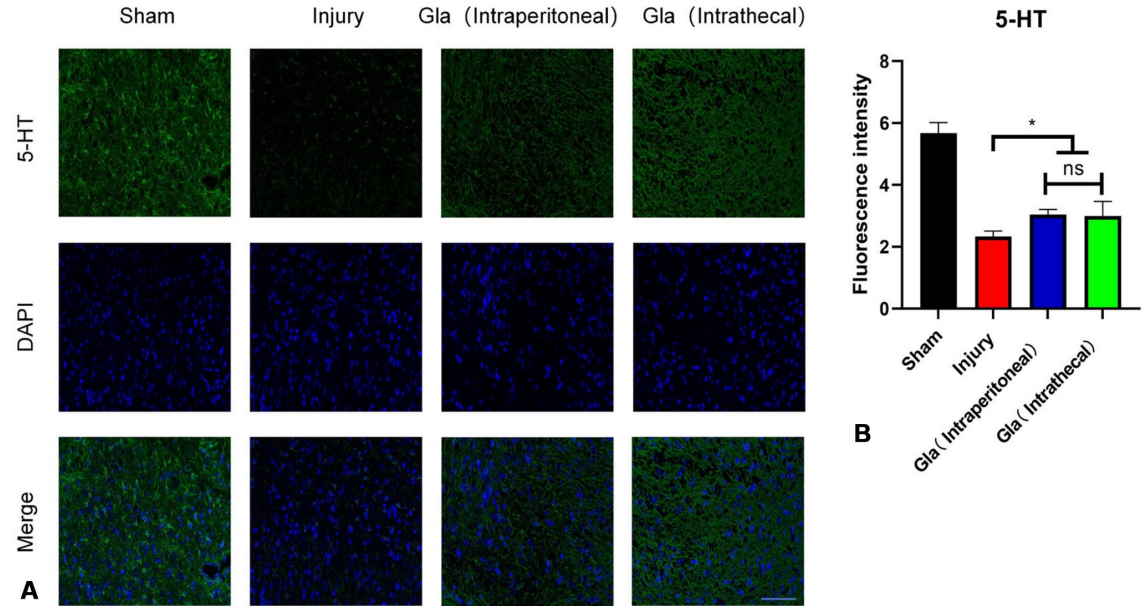

Fig. 6. 5-HT motor neuron generation. A: Immunofluorescence labeling analysis of axonal growth at 5-HT (green) after 6 weeks of treatment. Nuclei are stained with DAPI (blue). Scale bar = 50 mm. B: The quantitative analysis data of the fluorescence intensity of 5-HT positive axons are presented as the mean ± SD (n=5). *P < 0.05.

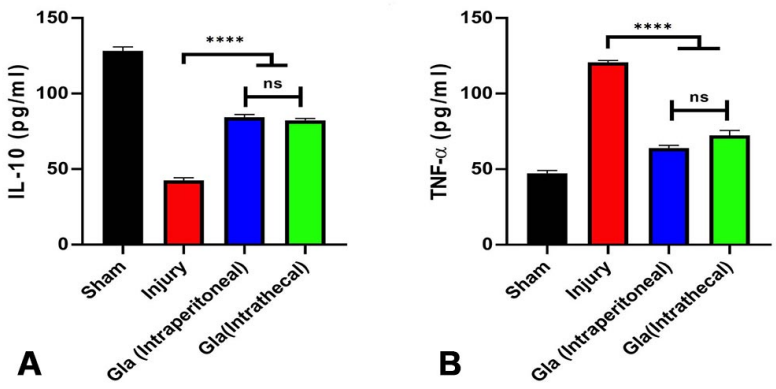

Fig. 7. Effect of intraperitoneal injection of Gla on the inflammatory response in mice with SCI. A: ELISA analysis of TNF-a levels in peripheral serum of SCI mice. B: ELISA analysis of IL-10 in the peripheral serum of mice with SCI. Data are presented as the mean ± standard deviation (n=5). ****P < 0.0001.

DISCUSSION

Traumatic SCIs occur mostly in young and middle-aged individuals. It results in significant detriment to individuals, entails substantial expenses for treatment, leads to enduring impairment in patients, and imposes a considerable economic strain on society. Therefore, minimizing the treatment cost is important while promoting the rehabilitation of patients with SCI. Gla is a licorice-derived natural compound with a variety of pharmacological activities and a wide array of natural sources and is known for its favorable safety profile. The clinical significance of Gla led us to investigate its potential therapeutic applications in the treatment of SCI. The intrathecal administration technique in rodents holds significant importance in the realm of investigating drug effects, specifically at the level of the spinal cord. Many investigators use direct intrathecal injections with low interference factors (Mestre *et al*., 1994; Tator, 1995). This study evaluated the reparative effects of Gla in SCI and compared the therapeutic efficacies of intraperitoneal and intrathecal injections.

Prolonged paralysis following SCI can lead to various complications. Hence, the restoration of motor function serves as a crucial indicator for assessing the efficacy of SCI repair. To assess the motor function restoration in the mice with SCI, we conducted measurements of the BMS scores at predetermined intervals. With the exception of the mice in the sham cohort, all other mice experienced paralysis immediately following the surgical procedure. During the 6-week observation period, the BMS score in the injured cohort failed to reach 4 points, indicating weak compensatory recovery after SCI. The BMS scores exhibited a gradual increase over time within the treatment cohort receiving Gla. Starting from the fourth week following the surgical procedure, the mice belonging to the treated cohort exhibited significantly higher scores compared to those in the injured cohort. The oblique experiment showed better recovery in each cohort, likely because the forelimbs fixed the body during the experiment. In general, intrathecal injections exhibited a tendency towards enhanced recovery, possibly because the drug can act directly on the injury site via the cerebrospinal fluid.

MRI and H&E staining revealed the pathology of the SCI. Physical injury early after SCI directly causes necrosis or apoptosis of astrocytes, oligodendrocytes, and neurons. The primary injury changes the microenvironment of the spinal cord parenchyma. In the later stage, a cascade is initiated, further causing secondary damage, aggravating damage to the nerve tissue, and expanding the injured area (Kaneko & Tsuchiya, 1954; Sadowsky *et al*., 2002; Bartanusz *et al*., 2011). The histopathological structure of mice treated with Gla exhibited greater regularity, indicating that Gla treatment has a positive effect on the cellular and tissue composition following SCI. The preservation of myelin structures is crucial for the proper functioning of nerve cells, and the demyelination extent in nerve cells following SCI is directly correlated with the injury severity. The LFB staining analysis conducted on the spinal cord tissue revealed the presence of demyelination in all experimental cohorts when contrasted to the sham cohort. However, the administration of intrathecal Gla injection successfully maintained the integrity of myelin.

In the central nervous system, astrocytes are the most common type of glial cell. The occurrence of glial scar formation following SCI can impede the process of spinal cord regeneration and repair, thereby hindering sustained functional activity (Lee *et al*., 1990). Gla inhibits gliosis and improves symptoms in Parkinson's mice. In this study, the level of GFAP in mice treated with an intrathecal injection of Gla was significantly less than that in the other cohorts, consistent with previous studies. Tuj1 is a tubulin protein involved in neuronal cell type-specific differentiation. Tubulin is the main component of microtubules, a component of the cytoskeleton, and plays roles in maintaining cell structure, mitosis, meiosis, and intracellular transport. Tuj1 is expressed in immature neuronal cell bodies (Smolinski & Pestka, 2003). Immunofluorescence staining showed that the intensity of Tuj1 elevated in the intrathecally-injected cohort relative to the other cohorts. This finding may predict the neurogerminal enhancement following scar inhibition. A comparison of 5-HT neurons in the treatment cohort with those in the injured cohort revealed that although immature

neurons regenerated less in the intraperitoneal cohort than in the intrathecal cohort, the intensity of 5-HT was slightly greater in the intrathecal cohort. This finding contrasts with our scenario.

Axonal regeneration may be related to an attenuated inflammatory response and reduced scar tissue. Gla showed excellent anti-inflammatory activity both in vitro and *in vivo*. Lipopolysaccharide (LPS) can change the amino acid metabolism, energy metabolism, and lipid metabolism patterns of macrophage RAW264.7, but Gla can reverse some of the LPS-induced changes (Zhang *et al*., 2017). In the LPS-induced RAW264.7 cell inflammation model, Gla downregulated cellular NO levels at low doses (10 μg/mL) and inhibited production by IL-1β (Kang *et al*., 2005). In LPS-induced acute respiratory distress syndrome in rats, Gla downregulated TNF-α and IL-18 by inhibiting the p38MAPK/ERK signaling pathway and reduced the production of malondialdehyde and NO, reducing inflammation and alleviating the lung injury (Kang *et al*., 2005).

Gla was also protective against the elevation of plasma NO synthase and TNF-α in mice after LPS induction (Kang *et al*., 2005). Therefore, Using ELISA, we assessed the concentrations of proinflammatory factors in the peripheral serum of SCI mice. Treatment with Gla decreased the expression of the proinflammatory factor TNF-α but elevated the IL-10 level, suggesting that Gla modulates the systemic inflammatory response in patients with SCI. Although more intensive studies are required, Gla exhibits promising clinical potential as a cost-effective dietary phytochemical. In subsequent studies, we intend to explore the underlying mechanism.

CONCLUSION

Gla, a cost-effective natural compound, can be readily extracted. Our results indicated that Gla treatment improves motor function and the pathological environment at the injury site. Gla treatment promoted the retention and reduced glial scar of Tuj1 and 5-HT neurons. Gla treatment also reduced serum TNF-α levels and elevated serum IL-10 levels. Our outcomes indicate that the reduction of systemic inflammatory responses mediated by Gla is associated with the restoration of motor function after SCI and that it may be a potential agent for treating SCI.

ETHICS APPROVAL

Yangzhou University's Animal Experimental Ethics Committee approved this study (yzu-lcyxy-n143/Jan 15, 2023). According to Yangzhou University Laboratory standards, feeding and welfare tests were conducted on the animals. Experiments pertaining to animal husbandry and welfare were carried out in accordance with the established protocols of the laboratory at Yangzhou University.

ZHAN, W.; FAN, Z.; TAO, J.; XING, Q.; BAO, X.; YAO, X. & CAI, J. Influencia del tratamiento con glabridina en la recuperación de la función motora después de una lesión de la médula espinal. *Int. J. Morphol., 42(3)*:709-717, 2024.

RESUMEN: La lesión de la médula espinal (LME) generalmente surge de la compresión producto de caídas y accidentes de tránsito, lo que resulta en alteraciones del movimiento, pérdida sensorial y posible parálisis. La Glabridina (Gla) es un compuesto natural derivado del regaliz, constituyéndose en un aporte significativo para el desarrollo de fármacos y la medicina debido a sus propiedades antiinflamatorias, antioxidantes, antitumorales, antibacterianas, osteoprotectoras, cardioprotectoras, neuroprotectoras, hepatoprotectoras, antidiabéticas y contra la obesidad. En el presente trabajo se emplearon varios métodos para administrar Gla a ratones con lesión medular con el fin de investigar su impacto en la recuperación de la función motora. Los ratones fueron distribuidos en cuatro grupos mediante un procedimiento de aleatorización. En el grupo simulado, únicamente se expuso quirúrgicamente la lámina del arco vertebral sin causar ningún daño al tejido de la médula espinal. Por el contrario, el grupo lesionado fue sometido a daño del tejido de la médula espinal, sin recibir tratamiento posterior. Los ratones de los dos grupos restantes recibieron una dosis de 40 mg/kg de Gla cada dos días mediante inyección intraperitoneal o intratecal durante 42 días después de la lesión de la médula espinal. Fueron realizadas pruebas de comportamiento utilizando la puntuación de la escala Basso Mouse y técnicas de análisis de la marcha. Se emplearon imágenes por resonancia magnética y se aplicaron tinciones histológicas (Hematoxilina & Eosina) en muestras para evaluar la formación de tejido cicatricial. La inflamación sistémica en ratones se evaluó mediante el empleo de un ensayo inmunoabsorbente ligado a enzimas. Gla promovió la recuperación de la función motora en ratones después de una lesión medular y mejoró el entorno patológico en el área dañada. Estas alteraciones fueron más evidentes en ratones sometidos al método de inyección intratecal. Las inyecciones intraperitoneales parecen ser más beneficiosas para controlar las respuestas inflamatorias sistémicas. Aunque se requieren estudios más intensivos, Gla exhibe un potencial clínico prometedor como fitoquímico dietético rentable.

PALABRAS CLAVE: Glabridina; Función motora; Lesión de la médula espinal; Neuroprotección.

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