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Repairing effect of Schwann cells combined with mesenchymal stem cells on optic nerve injury in rats

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Abstract. – **OBJECTIVE:** To investigate the effect and the underlying mechanisms of combined transplantation of Schwann cells (Scs) and Mesenchymal stem cells (MSCs) on optic nerve injury in rats.

MATERIALS AND METHODS: A total of 160 normal healthy adult rats were randomly divided into 4 groups: optic nerve injury group, optic nerve injury + Sc transplantation group, optic nerve injury + MSC transplantation group and optic nerve injury + Sc + MSC transplantation group. The optic nerve in the left eye of each rat was damaged via clamping to establish a model of optic nerve injury, and the right eye was used as self-control. Scs + MSCs, Scs alone, MSCs alone and normal saline were injected into the vitreous space, respectively. After the treatment, the optic nerve tissues were collected and subjected to hematoxylin-eosin (HE) staining. Next, the morphologic and pathological changes of rats in each group were observed. Retrograde labeling was utilized to count the number of retinal ganglion cells (RGCs) in the optic nerve tissues. The apoptosis of RGCs was detected using flow cytometry. Western blot was carried out to measure the protein expression level of B-cell lymphoma 2 (Bcl-2) and Bcl-2-associated X protein (Bax). The expression and distribution of brain-derived neurotrophic factor (BDNF) and growth associated protein-43 (GAP-43) in the optic nerve of rats in each group were detected by immunohistochemistry.

RESULTS: Transplantation of Scs and MSCs could maintain the morphological structures of the retina and optic nerve of rats, increase the amount of RGCs in optic nerve tissues, reduce the apoptosis of RGCs, promote the expression of the Bcl-2 protein and decrease the expression of Bax protein. In addition, our joint transplantation strategy also showed an important role in repairing optic nerve injury by clearly promoting the secretion and expression of BDNF and GAP-43, which indicated a better curative effect than that of separate application of Scs or MSCs.

CONCLUSIONS: Therapy with combined use of Scs and MSCs has a significant therapeutic effect in repairing optic nerve injury.

Key Words

Schwann cells, Bone marrow mesenchymal cells, Optic nerve injury, RGCs, BDNF, GAP-43.

Abbreviations

Scs: Schwann cells, MSCs: mesenchymal stem cells, RGCs: retinal ganglion cells, HE: hematoxylin-eosin, Bcl-2: B-cell lymphoma 2, Bax: Bcl-2-associated X protein, BDNF: brain-derived neurotrophic factor, GAP-43: growth associated protein-43, DMEM: Dulbecco's modified Eagle medium, PI: propidium iodide, RIPA: radioimmunoprecipitation assay, BCA: bicinchoninic acid, GAPDH: glyceraldehyde-3-phosphate dehydrogenase, BDNF: brain-derived neurotrophic factor, GAP-43: growth associated protein-43, IgG: immunoglobulin G, SABC: streptavidin-biotin complex, PBS: phosphate-buffered saline, SDS-PAGE: sodium dodecyl sulfate-polyacrylamide gel electrophoresis, TBST: Tris-buffered saline with Tween-20, ECL: enhanced chemiluminescence, DAB: diaminobenzidine, AOD: average optical density, SPSS: Statistical Product and Service Solutions, ANOVA: One-way analysis of variance.

Introduction

Optic nerve injury is a common type of ocular trauma and also a cause of blindness in clinical practice. The regeneration of the optic nerve system is difficult because of its poor self-repairing function. The effects and prognoses of current therapies are often hard to reach the expectations[1]. Therefore, finding new treatment methods for optic nerve injury is a hotspot and also a difficulty

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in current ophthalmology. Studies have shown that optic nerve is mainly composed of the axons of retinal ganglion cells (RGCs) and the secondary loss of RGCs is the main pathological cause of impaired visual function after optic nerve injury. Thus, the survival and axonal regeneration of RGCs after injury are keys to repair neuronal injury[2,3]. Schwann cells (Scs) play important roles in nerve regeneration. It is reported that Scs can secrete various neurotrophic factors, thereby repairing peripheral nerve injury and promoting regeneration[4,5]. Stem cell transplantation therapy is a hotspot in current medical research, which is widely used in the treatment of tissue damage. Mesenchymal stem cells (MSCs) are a class of stem cells with multi-lineage differentiation potential and low antigenicity. Scholars have indicated that MSCs can differentiate into a variety of neurocytes *in vitro* and *in vivo*, exerting an active influence on nerve injury repair[6]. High sensitivity to injury and lack of compensatory Scs make optic nerve a poor self-repairing ability and difficult to be repaired after injury[7]. In consideration of the therapeutic effect of MSCs and the characteristics of Scs, this study established rat models of optic nerve injury to study the pathophysiological impact and to repair function of the combined application of Scs and MSCs, thereby providing new insights for the treatment of optic nerve injury in the future.

Materials and Methods

Experimental Animals and Cells

A total of 160 healthy male Wistar rats aged 2-3 months old and weighing approximately 200-250 g were purchased from the Experimental Animal Center of Qingdao University. This study was approved by the Animal Ethics Committee of Qingdao University Animal Center. These rats were fed adaptively in this laboratory for one week with free access to food and water under the environment of 12 h light/12 h dark. The results of both routine external ocular examination and fundus examination were normal. Models of optic nerve crush injury were established in left eyes, while right eyes were used as self-control.

Rat Scs RSC96 and primary MSCs were purchased from the cell bank of Shanghai Institute of Biochemistry and Cell Biology (Chinese Academy of Sciences), resuscitated in our laboratory and used in subsequent experiments.

Reagents

Reagents used in this study were as follows: Eosin-hematoxylin (H&E) staining solution (purchased from Beyotime Biotechnology, Beijing, China), paraformaldehyde (bought from Sigma-Aldrich Corporation, St. Louis, MO, USA), erythromycin eye ointment (purchased from Southwest Pharmaceutical Co., Ltd., Chongqing, China), pentobarbitone sodium (bought from Sinopharm Co., Ltd., Shanghai, China), fetal bovine serum and Dulbecco's Modified Eagle Medium (DMEM) (bought from Hyclone, South Logan, UT, USA), biotin dextran amine (BDA-10000) (purchased from Sigma-Aldrich Corporation, Saint Louis, MO, USA), Annexin-V antibody and propidium iodide (PI) antibody (purchased from Beyotime Biotechnology, Beijing, China), radio immunoprecipitation assay (RIPA) cell lysis solution and bicinchoninic acid (BCA) kit (bought from Wuhan Boster Biological Technology Co., Ltd. Wuhan, China), rabbit anti-rat B-cell lymphoma 2 (Bcl-2), Bcl-2-associated X protein (Bax), glyceraldehyde-3-phosphate dehydrogenase (GAPDH), brain-derived neurotrophic factor (BDNF), growth associated protein-43 (GAP-43) primary antibodies (bought from Abcam, Cambridge, MA, USA), goat anti-rabbit immunoglobulin G (IgG) second antibody (purchased from Beijing Zhongshan GoldenBridge Biotechnology Co., Ltd. Beijing, China), streptavidin-biotin complex (SABC) immunohistochemistry kit (bought from Shanghai Sangon Biotech, Shanghai, China).

Methods

Establishment of Rat Models of Optic Nerve Crush Injury

All rats were anesthetized by intraperitoneal injection of pentobarbital sodium (3 mL/Kg), and then kept in prone position and fixed on an operating table. Under an operating microscope, the left eye's upper fornical conjunctiva was incised approximately 120° along the corneal limbus, and the conjunctiva was bluntly dissected to the sclera. When backward dissection was carried out, vortex veins should be kept away. After 4 mm retrobulbar optic nerve was exposed, the optic nerve was clamped using a non-invasive medium serrefine at 2 mm behind the eyeball for 10-15 s, avoiding damaging ophthalmic artery. For the control eye, the optic nerve was exposed without clamping. After the operation, the cornea was lightly pressed with a slide, and the fundus

was observed under the operating microscope. Rats without ischemia after the operation were included in the experiment. Stratified suture was performed after the operation, and rats were sent to the Animal Center for feeding. Their eyes were treated with erythromycin eye ointment.

Cell Processing and Animal Grouping

Rat Scs RSC96 and primary MSCs were resuscitated and cultured with DMEM containing 15% fetal bovine serum. Then, the state of cells was observed under an inverted microscope and cells in good state were selected for subsequent transplantation experiments. Rats with optic nerve injury were randomly divided into four groups: optic nerve injury model group (intravitreal injection of 10 μL normal saline after the optic nerve of rats was injured, Model group), optic nerve injury + SC transplantation group (intravitreal injection of 10 μL 10^7/mL Scs after rat models of optic nerve injury were established for 12 h, Scs group), optic nerve injury + MSC transplantation group (intravitreal injection of 10 μL 10^7/mL MSCs at 12 h after rat models of optic nerve injury were established, MSCs group), optic nerve injury + SC + MSC transplantation group (intravitreal injection of 5 μL 10^7/mL Scs and 5 μL 10^7/mL MSCs after 12 h of establishment of rat models of optic nerve injury, Scs + MSCs group).

Detection of the Damage of Optic Nerve Tissue via H&E Staining

At 3rd d, 1st W and 2nd W after treatment, 5 rats in each group were selected and sacrificed *via* dislocation. Eyeballs were removed immediately by aseptic operation with optic nerves retained. Eyeballs and optic nerves were promptly fixed in 4% formaldehyde solution for 12 h. Then, the eyeball was dissected in half along the corneal apex and the lateral edge of the optic disc and the bitemporal hemisphere was dehydrated with graded alcohol, embedded and sectioned. After that, H&E staining was performed, and the changes in optic nerve system tissues (the retina and optic nerve) of rats in different groups were observed under an optical microscope.

Counting of RGCs

Biotin dextran amine (BDA-10000) was dissolved in 0.5 mL of normal saline to prepare into 50 mg/mL BDA. Then, BDA was injected into vitreous bodies, bilateral geniculate bodies and superior colliculi of rats in each group 3 days before material collection, and RGCs were subjected to retrograde labeling. Eyeballs were fixed with 4% paraformaldehyde for 5 h before being incised along 0.5 mm away from the edge of the cornea, and the lens and the cornea were then removed. The retina was obtained after separation, spread on a glass slide, and mounted with glycerinum. After that, the retina was observed under a fluorescence microscope and photographed at 1/6, 3/6, and 5/6 away from the papilla nervi optici in 4 retinal quadrants, respectively, followed by 4 times of random and continuous observation. Lastly, RGC counting was conducted.

Determination of Apoptosis of RGCs through Flow Cytometry

Totally 3 days after transplantation, 5 rats in each group were randomly sacrificed and injured eyeballs were aseptically removed at once. Then, the retina was dissected under an operating microscope and gently ground and dissociated by a grinder to prepare retinal cell suspension. After that, the retinal cell suspension was added with 500 μL of Binding Buffer, 5 μL of fluorescein isothiocyanate (FITC)-labeled Annexin-V antibody and PI antibody for incubation in a dark place at room temperature for 30 min. A BD Calibur flow cytometer (BD Company, Franklin Lakes, NJ, USA) was used to detect the apoptosis of RGCs in cells in each group.

Measurement of Bax and Bcl-2 Expression Levels in the Optic Nerve Tissue by Western Blotting

After the above-isolated eyeballs of rats in each group were taken out, the optic nerve tissue was separated and removed under a microscope, followed by washing with PBS. Then, the optic nerve tissue was added with 500 μL radioimmunoprecipitation assay (RIPA) strong cell lysis solution, ground and mixed. After that, the total protein in the optic nerve tissue was extracted and the bicinchoninic acid (BCA) kit was utilized to measure the concentration of the total protein. Next, 30 μg protein of each group was loaded and separated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) for 1.5 h before transferred to a polyvinylidene difluoride (PVDF) membrane (Millipore, Billerica, MA, USA). After that, the membrane was blocked with 5% nonfat dry milk for 20 min. Then, the membrane was incubated with rabbit anti-mouse Bcl-2, Bax and GAPDH primary antibodies (1:1000) at 4°C overnight. After being washed in Tris-Buffered Saline with Tween-20 (TBST) three times,

the membrane was then incubated with goat anti-rabbit IgG secondary antibody (1:5000) at room temperature for 2 h, followed by washing with TBST 3 times. Thereafter, 1 mL of enhanced chemiluminescence (ECL) reagent was added for color development. Bio-RAD gel exposure imaging system was applied for exposure, development and imaging. Quantity One software was employed to analyze the relative protein expression levels of Bcl-2 and Bax.

Detection of Expression Levels of BDNF and GAP-43 in Optic Nerve Tissue in Each Group via Immunohistochemistry

After 2 weeks of different cell transplantations in rats in each group, 5 rats in each group were randomly sacrificed. The injured eyeballs were collected and the optic nerve tissue was carefully peeled off under the microscope, fixed with 4% paraformaldehyde, dehydrated in graded alcohol, embedded in paraffin and sectioned. After that, the tissues were dewaxed, rehydrated, heat-induced antigen extracted, serum blocked and incubated with rabbit anti-rat BDNF and GAP-43 primary antibodies (1:500) at room temperature for 2 h. After being washed 3 times, the sections were incubated with a secondary antibody with the addition of biotinidase labeled working solution. Color development with diaminobenzidine (DAB) according to the instructions of the SABC immunohistochemistry kit (San Antonio, Texas, USA). Thereafter, the optic nerve tissue was observed and photographed under the microscope. The average optical density (AOD) was calculated based on positive results on the immunohistochemical images in each group using Image-Pro Plus software (Rockville, MD, USA).

Statistical Analysis

Statistical Product and Service Solutions (SPSS) 13.0 software (Chicago, IL, USA) was used for statistical analyses. The results were expressed as mean ± standard deviation (SD). Independent Student *t*-test was used for comparisons between the two groups. One-way analysis of variance (ANOVA) was adopted for comparisons among multiple groups, followed by Post Hoc Test (Least Significant Difference). $p<0.05$ suggested that the difference was statistically significant.

Results

Establishment and Detection of Optic Nerve Injury Models

In this study, rat models of optic nerve injury were successfully established using optic nerve crush method (Figure 1A). H&E staining was carried out to display the damage of the optic nerve tissue in rats. The results suggested a clear structure of three cell layers, which included the photoreceptor cell layer, the bipolar cell layer and ganglion cell layer. According to the H&E staining of the optic nerve tissues, nerve fiber tissue was arranged precisely and neatly (Figure 1B). Compared to the normal tissues, the cellular structure of the retina in each layer became disorganized, and the photoreceptor cell layer and the ganglion cell layer became thinner at the 14th day after the injury. Moreover, in the optic nerve tissue, the number of RGCs were decreased significantly and the nuclei were arranged disorderly. Cavitated ganglion cells and infiltrating inflammatory cells also appeared. The above results indicated that our rat optic nerve injury model has been established successfully (Figure 1C).

Preparation of Scs and MSCs

Resuscitated Scs and MSCs were cultured in DMEM containing 15% fetal bovine serum and observed under the inverted microscope. Scs grew in adhesive form with long spindle shape and prominent at both ends. The growth and micromorphology of MSCs were also confirmed to

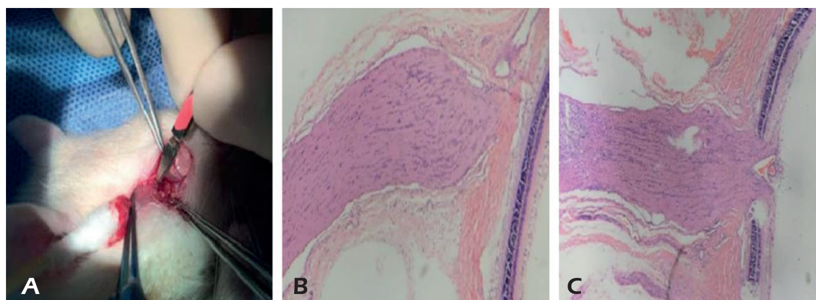

Figure 1. Construction and detection of rat models of optic nerve injury (From left to right: **A**, **B**, and **C**) (×200).

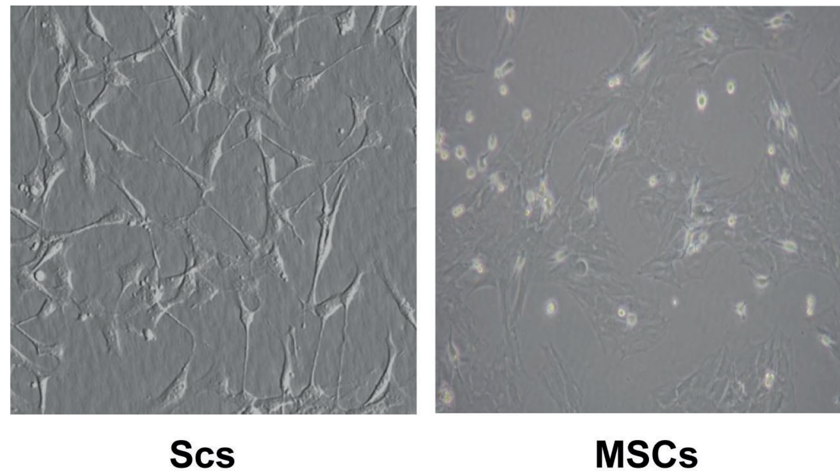

Figure 2. Culture of SCs and MSCs (Left: Scs, right: MSCs) (×200).

be qualified (Figure 2). Scs and MSCs were then seeded and used immediately for subsequent cell transplantation experiments.

Pathological Changes in the Retina and Optic Nerve of Rats in Four Groups Detected via H&E

The changes in the morphological structure of the retina were detected through H&E staining (Figure 3). Retina tissue of rats in injury group exhibited chaotically arranged cells with severe necrosis, overtly reduced RGCs in number, largely decreased number of photoreceptor cells in the inner nuclear layer, cavitated ganglion cells and sparse nuclei (Figure 3A). However, rats in Scs group had increased number of nuclei and photoreceptor cells in the inner nuclear layer, as well as more neatly arranged RGCs cells and reduced cavitation of ganglion cells in the retina (Figure 3B). Consistent with expectations, rats in the MSCs group showed similar reduced retinal damages to those in Scs group (Figure 3C). The retinal struc-

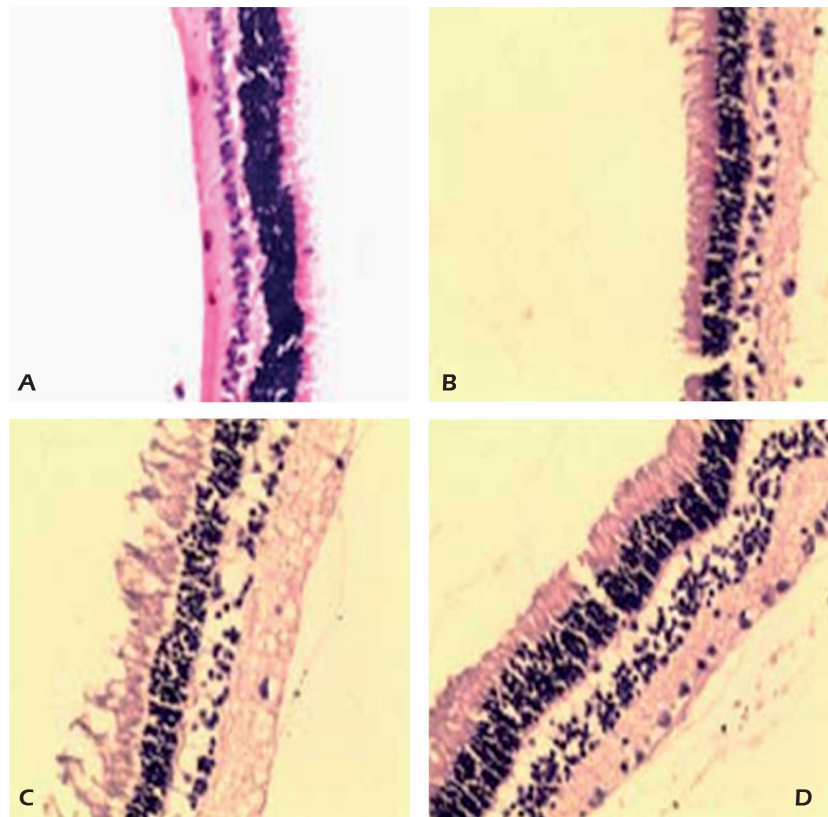

Figure 3. Pathological changes in retina of rats detected via H&E staining (×400) (From left to right and top to bottom: **A**, Model group, **B**, Scs group, **C**, MSCs group and **D**, Scs + MSCs group).

tures of injured optic nerves of rats in Scs + MSCs group were clearer and more complete than the other three groups. RGCs were neatly arranged, ganglion cells, as well as the photoreceptor cells, in the inner nuclear layer were increased significantly in number, and the distribution of nuclei became uniform (Figure 3D). All of these indicated that the morphology of the damaged retina of rats in Scs + MSCs group had a better recovery.

Besides, the pathological changes of optic nerve tissue of rats were also observed (Figure 4). In the injury group, the fiber structure of the optic nerve was distorted. The optic nerves were significantly shrunken and deformed, almost all of the marginal cells were vacuolated and neurons were sparse (Figure 4A). In Scs group, although the fiber structure was still irregular, the vacuolated cell was markedly reduced and the number of RGCs was increased (Figure 4B). In MSCs group, the number RGCs significantly increased, optic nerve fibers were arranged neatly and vacuolated cells were also reduced (Figure 4C). In the Scs + MSCs group, the number of RGCs was significantly higher than those in Scs group and MSCs group. The nerve fibers were well arranged and the morphology of the optic nerve was well restored (Figure 4D).

Results of RGS Counting

After the retina of rats with optic nerve injury was subjected to retrograde labeling with BDA, RGCs were observed and counted under the fluorescence microscope (Figure 5). It was found that the number of RGCs in the retina of rats with optic nerve injury in the injury group was significantly reduced, while it is significantly increased in the other three groups. Surprisingly, the number of RGCs in the Scs + MSCs group was significantly higher than in the Scs group and MSCs group.

Results of the Apoptosis of RGCs in Rat Optic Nerve Tissues Detected by Flow Cytometry

Flow cytometry was used to detect the apoptosis of RGCs in the optic nerve of rats in each group after transplantation with different cells. The results showed that the apoptosis of RGCs in the optic nerve was decreased in Scs group, MSCs group and Scs + MSCs group compared to the injury group (Figure 6). Besides, the apoptosis rate of RGCs in Scs + MSCs group showed a more significant decline compared to that of the Scs group and MSCs group.

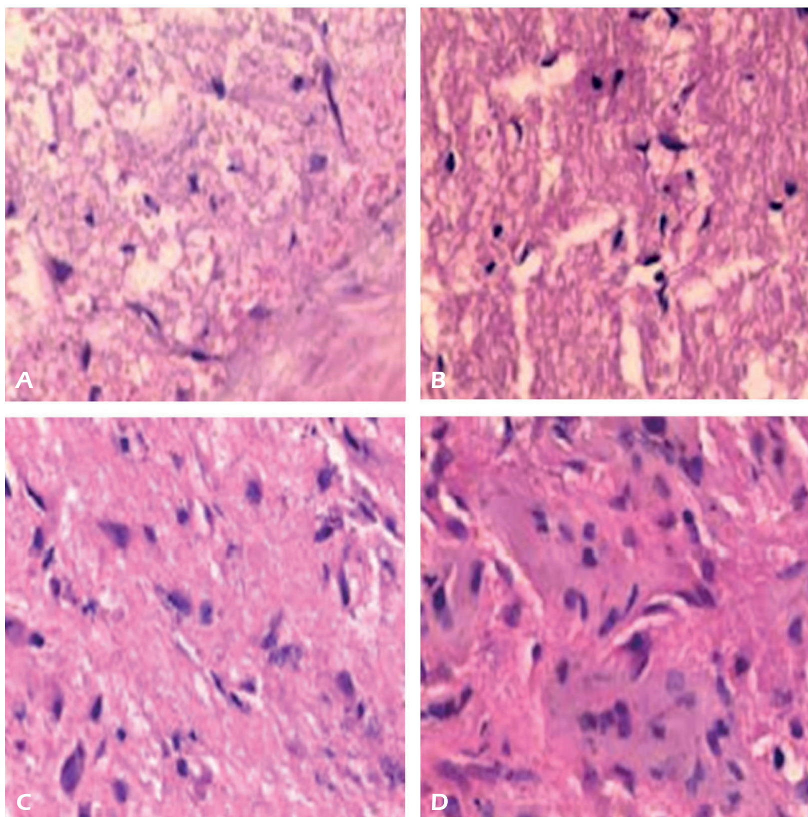

Figure 4. Pathological changes in optic nerve of rats detected via H&E (×400) (From left to right and top to bottom: **A**, Model group, **B**, Scs group, **C**, MSCs group and **D**, Scs + MSCs group).

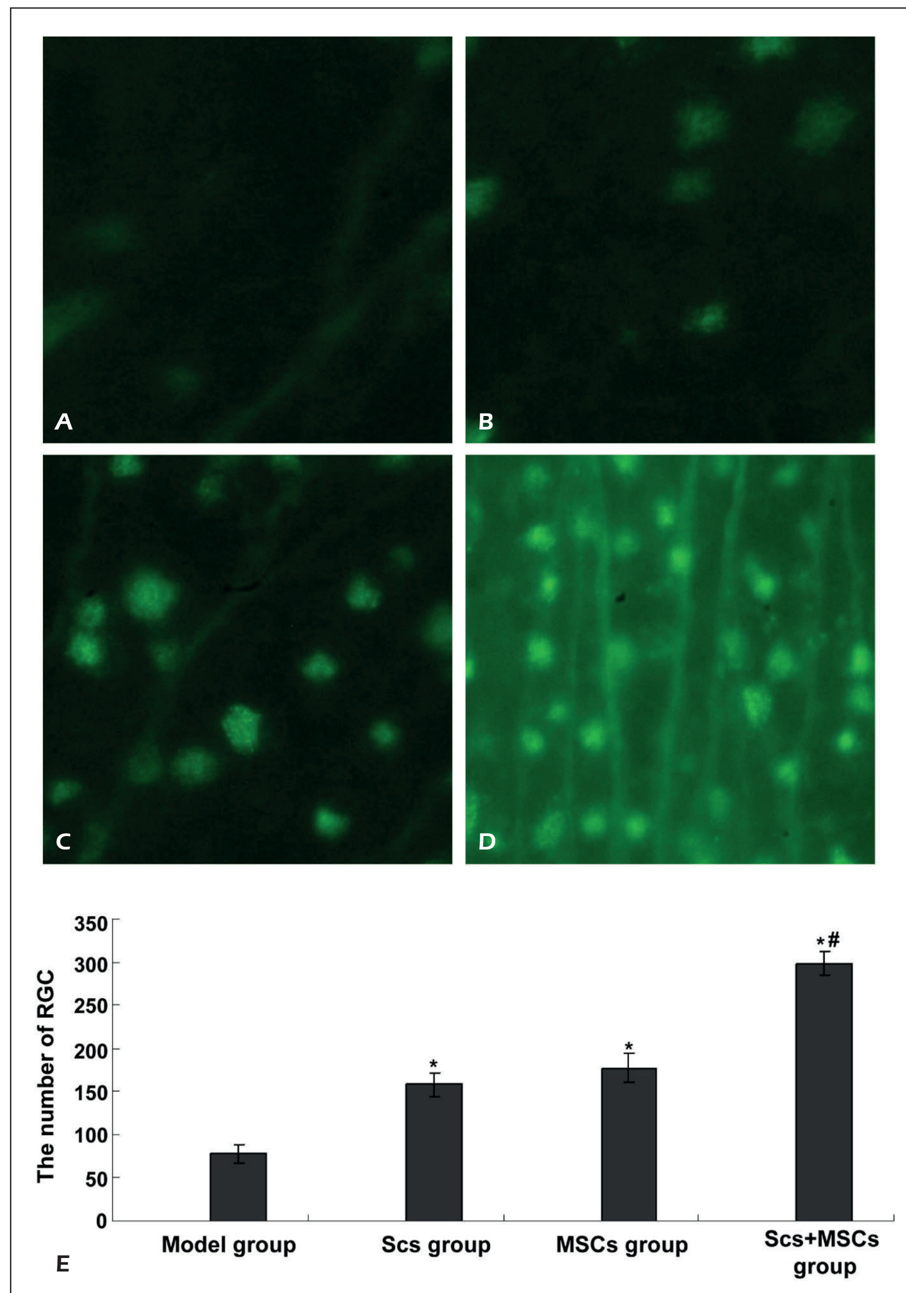

Figure 5. BDA retrograde labeled RGCs in nerve tissues of the retina of rats in each group (Mean ± SD. n=5) (×400, from left to right and top to bottom: model group, Scs group, MSCs group and Scs + MSCs group). Compared with Model group, *p<0.05, compared with Scs group and MSCs group, $^{\#}p$<0.05.

Protein Expression Levels of Bax and Bcl-2 in the Optic Nerve Tissue of Rats in Each Group Detected through Western Blotting

Western blotting analyses suggested that the protein expression level of Bax in the Scs group, MSCs group and Scs + MSCs group was markedly decreased compared to that in the injury group, while the Bcl-2 expression showed a remarkable increase (Figure 7). In addition, the co-transplantation of Scs and MSCs showed stronger inhibitory effect on Bax expression and a better promoting effect on Bcl-2 expression than the single cell transplantation.

Expression Levels of BDNF and GAP-43 in Optic Nerve Tissue of Rats in Each Group Measured by Immunohistochemistry

The expression and distribution of BDNF and GAP-43 in the optic nerve tissue of rats with optic nerve injury were detected by immunohistochem-

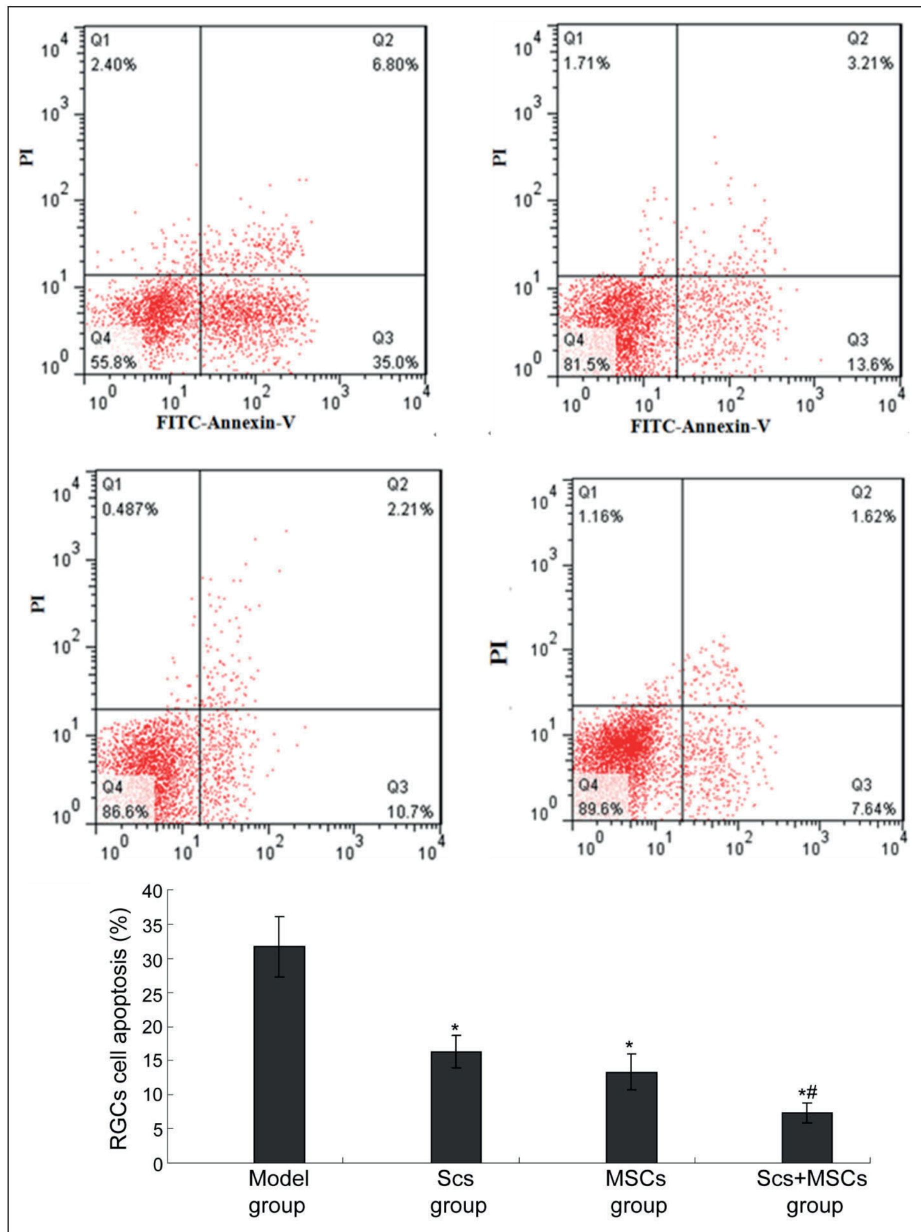

Figure 6. Apoptosis of RGCs in rat optic nerve tissues in each group detected by flow cytometry (Mean ± SD. n=5) (From left to right and top to bottom: model group, Scs group, MSCs group and Scs + MSCs group). Compared with Model group, *$p<0.05$, compared with Scs group and MSCs group, #$p<0.05$.

istry. As shown in Figure 8 and Figure 9, the optical density results of BDNF and GAP-43 positive expression in SCs group and MSCs group was significantly higher than that in the injury group, while it was lower than that in Scs + MSCs group (Figure 10).

Discussion

Clinical studies have found that optic nerve injury is caused by various eye diseases or some external stress, and many patients with optic nerve injury suffer from serious optic atrophy or even blindness[8]. The optic nerve system of mammals belongs to the central nervous system and consists of axons and optic nerve cells from RGC bodies. Scs was reported to proliferate and secrete a variety of neurotrophic factors, facilitating the survival of neurons and forming a connection in the injured area to promote the regeneration of axons. However, a lack of enough Scs makes the regeneration and repair of the optic nerve after injury relatively difficult[9,10]. The application of stem cells in repairing critical tissues is a hot topic in current medical research. Some scholars[11,12] have

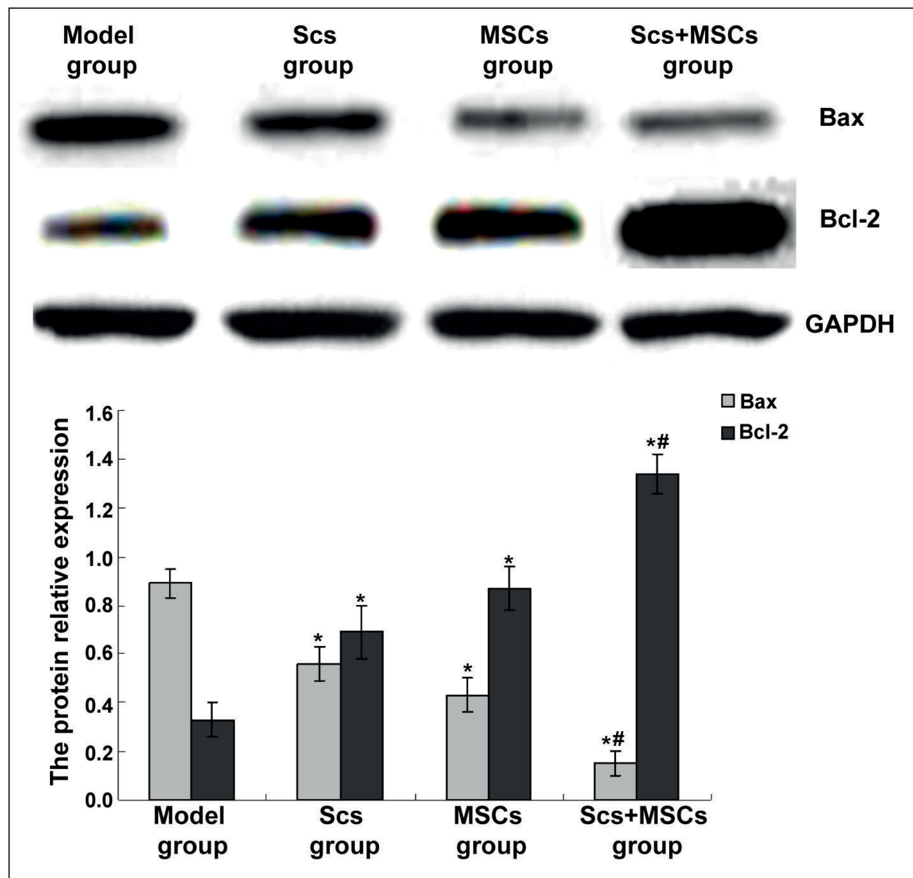

Figure 7. Protein expression levels of Bax and Bcl-2 in the optic nerve tissue of rats in each group detected through Western blotting (Mean ± SD. n=5). Compared with Model group, $*p<0.05$, compared with Scs group and MSCs group, $\#p<0.05$.

used MSCs in the repair of rat optic nerve with a crush injury, and have achieved satisfying results. Nevertheless, there is no research on the application of Scs in combination with MSCs in the optic nerve injury now. Considering the particularities of Scs in the optic nerve system and the promising curative effect of MSCs in nerve repair Scs and MSCs were separately or co-transplanted into rats with injured optic nerve. We found that the combined application of Scs and MSCs had an excellent repairing effect on optic nerve injury in rats, which was superior to that of separated use of Scs or MSCs.

Studies have implied that after the optic nerve is damaged by clamping, massive nerve fibers in the optic nerve tissue are not broken. However, the nerve myelin sheaths showed half-layer separation, disordered structure or even fracture, which is accompanied by axoplasmic fluid transport blocking and dysfunction of some axon points. As a result, RGCs are reduced in number[13,14]. In this study, the retrograde labeling used to capture RGCs in optic nerve tissue suggested that the number of RGCs in the injured optic nerve tissue was decreased significantly. The transplantation of Scs, MSC or Scs + MSCs significantly upregulated the RGCs number, and the co-transplantation of Scs and MSC showed a better effect in the repair of the optic nerve injury than just transplanting one kind of above cells. A report[15] showed that the apoptosis of RGCs in the optic nerve is one of the main cause of impaired visual dysfunction. The histological and pathological basis of optic nerve injury includes the reduction and apoptosis of RGCs and their axons. With the increase of the apoptosis of RGCs, it becomes more difficult to restore the function of the optic nerve[16]. In this work, flow cytometry analysis showed that the apoptosis of RGCs in the optic nerve of rats 3 days after injury (the early stage of optic nerve injury), while both Scs and MSCs could reduce the apoptosis rate of RGCs in the optic nerve. Bcl-2/Bax ratio can be used to reveal the progress of apoptosis[17,18]. Deng et al[9] demonstrated that the Bcl-2 and Bax protein expression plays an important role in the apoptosis of RGCs, and the ratio of Bcl-2/Bax is related to the decreased number of RGCs. In this study, the protein expression of Bcl-2 in the optic nerve was significantly increased in the Scs group, MSCs

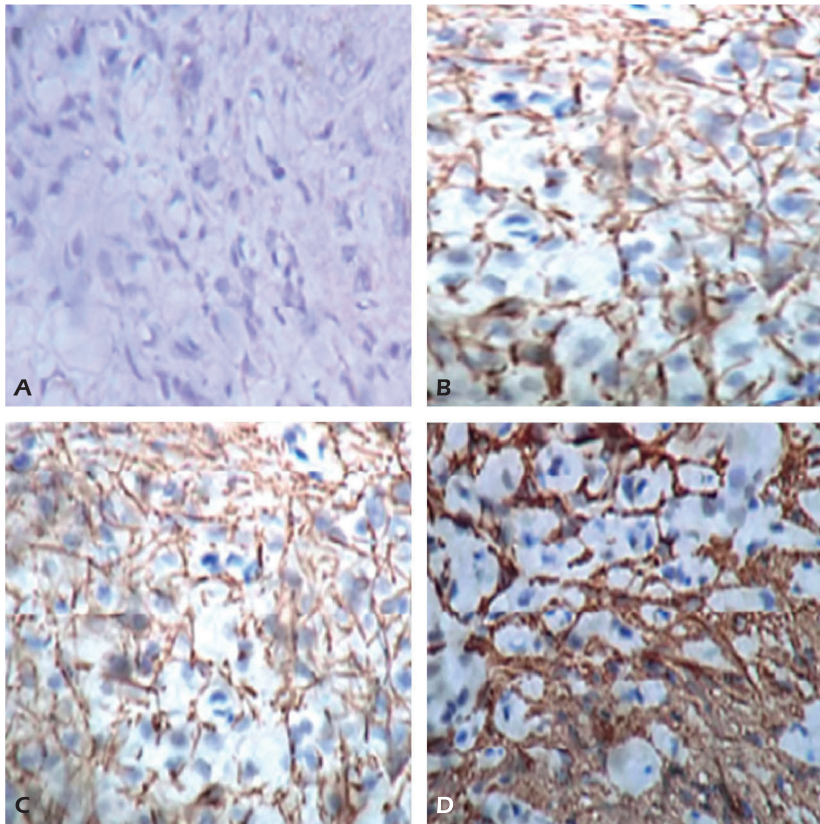

Figure 8. Distribution and expression of BDNF in the optic nerve tissue of rats in each group via immunohistochemistry (×400, from left to right and top to bottom: model group, Scs group, MSCs group and Scs + MSCs group).

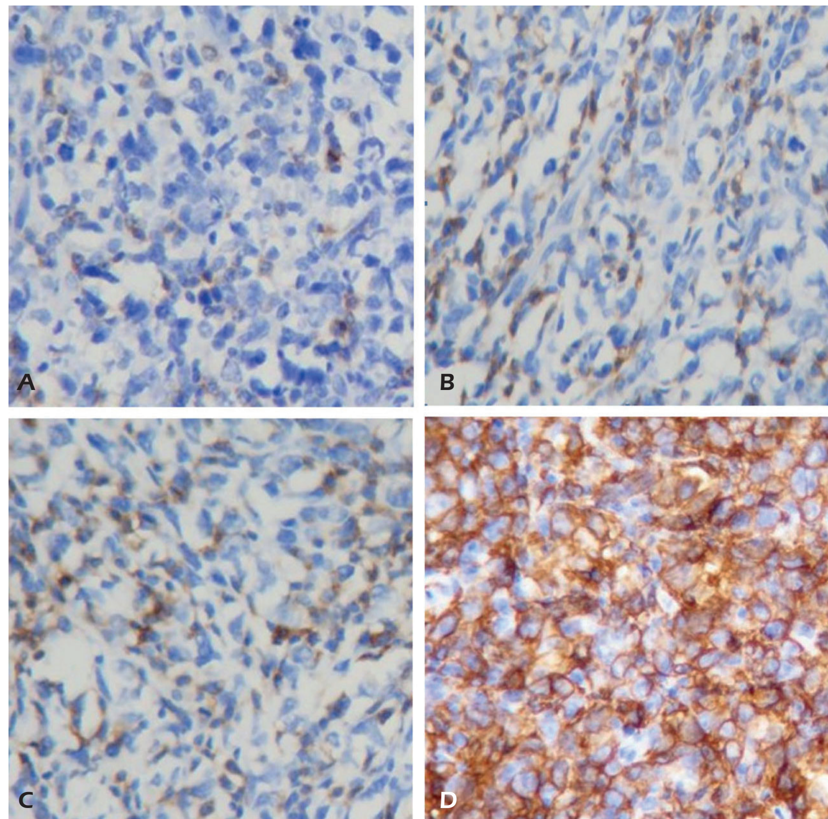

Figure 9. Distribution and expression of GAP-43 in the optic nerve tissue of rats in each group via immunohistochemistry (×400, from left to right and top to bottom: model group, Scs group, MSCs group and Scs + MSCs group).

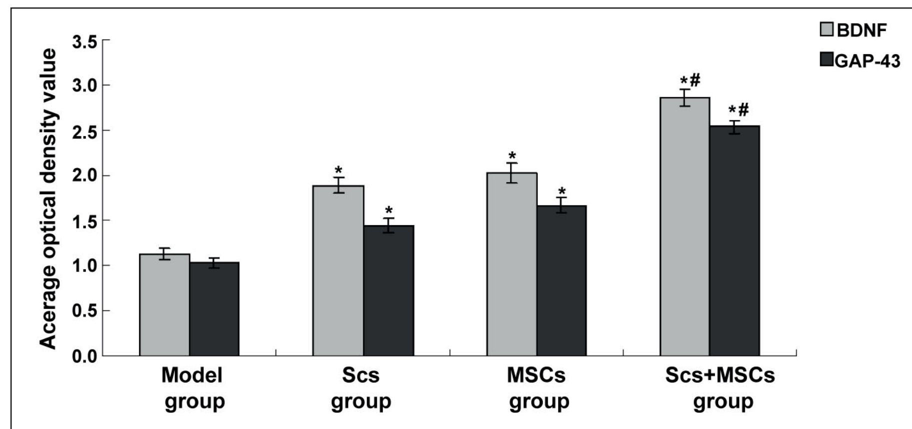

Figure 10. Optical density of the distribution and expression of BDNF and GAP-43 in the optic nerve tissue of rats in each group (Mean ± SD. n=5). Compared with Model group, *$p<0.05$, compared with Scs group and MSCs group, #$p<0.05$.

group and Scs + MSCs group compared to that in the injury group, while Bax was decreased. The above data indicated that the transplantation of Scs and/or MSCs inhibited the apoptosis of RGCs by regulating the ratio of Bcl-2/Bax.

The repair and regeneration of the optic nerve are complex processes that require the maintenance of relevant neurotrophic factors and changes in the microenvironment, so the supplementation of neurotrophic factors is emphasized in the clinical treatment of optic nerve injury[20]. Caminos et al[21] showed that treatment with MSCs has a definite curative effect, while the underlying mechanism is still unclear[21]. MSCs can interact with host nerve cells and promote the production of some neurogenic factors, including transforming growth factor and BDNF[22]. BDNF, a key nutrition factor in the nervous system, exists in the nervous system and plays important roles in the survival, differentiation and growth of neurons. It can improve the pathological state of the nervous system and promote the regeneration of damaged neurons[23]. GAP-43, a neural-specific phosphoprotein, is used as a molecular marker for neuronal growth, axon regeneration and plasticity[24]. It is reported that the re-expression of GAP-43 is one of the important activities of cells for the regeneration of optic nerve after RGC damage. Both BDNF and GAP-43 are important components in the development, extension and regeneration of optic nerve axons[25]. In this work, the positive expression of BDNF and GAP-43 in the optic nerve sections of rats in Scs group, MSCs group and Scs + MSCs group was markedly elevated compared with that in the injury group. Besides, the expression of BDNF and GAP-43 in Scs + MSCs group was higher than that in SCs group and MSCs group, indicating that co-transplanted Scs and MSCs might achieve the curative effect in the repair of rat optic nerve injury by promoting the secretion of neurotrophic factors like BDNF and GAP-43.

Conclusions

For the first time, we observed that the combined application of Scs + MSCs could promote the repair of the optic nerve injury in rats, and its therapeutic effect is better than that of separate use of Scs or MSCs, which provides new ideas and directions for the clinical treatment of the optic nerve injury.

Conflict of Interests

The authors declared no conflict of interest.

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