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Autogenous Fat Grafting and Platelet-Rich Plasma use to Enhance Nerve and Nerve Graft Regeneration; A Review Article

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Abstract: Autogenous fat grafting (AFG) and platelet-rich plasma (PRP) have emerged as promising regenerative therapies in peripheral nerve repair, particularly in the context of sciatic nerve injuries. The sciatic nerve, being the largest peripheral nerve in the body, is critical for motor and sensory function, and its regeneration remains a significant clinical challenge. This review article comprehensively examines the current evidence on the use of AFG and PRP in sciatic nerve graft regeneration, focusing on their mechanisms of action, efficacy, and potential synergies. AFG provides a scaffold rich in adipose-derived stem cells (ASCs) and growth factors, promoting angiogenesis, reducing fibrosis, and enhancing axonal regrowth. PRP, on the other hand, delivers a concentrated pool of growth factors and cytokines that modulate inflammation, stimulate cellular proliferation, and support tissue remodeling. Preclinical and clinical studies suggest that both AFG and PRP can significantly improve nerve regeneration outcomes, including functional recovery and histological evidence of axonal regrowth. Furthermore, combining these therapies may offer additive or synergistic benefits, enhancing the regenerative microenvironment. However, challenges such as standardization of protocols, optimal timing of application, and long-term outcomes remain to be addressed. This review highlights the potential of AFG and PRP as adjuncts to traditional nerve grafting techniques, offering new avenues for improving functional recovery in patients with sciatic nerve injuries.

Keywords: Sciatic Nerve Graft Regeneration, Autogenous Fat Grafting, Platelet-Rich Plasma

Introduction.

Peripheral nerve injuries (PNIs) are a significant clinical concern, often resulting from trauma, compression, or iatrogenic causes. Among these, injuries to the sciatic nerve are particularly debilitating due to the nerve's extensive distribution and crucial role in motor and sensory function in the lower limb [1]. The sciatic nerve, originating from the lumbosacral plexus (L4-S3), is the largest nerve in the human body and serves both motor

and sensory purposes, innervating muscles of the thigh, leg, and foot [2]. Damage to this nerve can result in significant disability, including foot drop, sensory loss, and neuropathic pain.

Traumatic sciatic nerve injuries are commonly associated with high-impact events such as motor vehicle accidents, gunshot wounds, or iatrogenic causes like hip surgeries [3]. Iatrogenic injuries remain a leading cause, particularly following hip arthroplasty or intramuscular injections in the gluteal region [4]. These injuries can vary in severity from neurapraxia, where the nerve's structure remains intact, to neurotmesis, where there is complete disruption of the nerve fibers [5]. Early diagnosis and intervention are critical to improving outcomes.

The pathophysiology of sciatic nerve injuries involves disruption of axonal transport, demyelination, or Wallerian degeneration, depending on the severity of the trauma [6]. Wallerian degeneration, in particular, involves the breakdown of the axon and myelin distal to the injury site, leading to loss of neural transmission [7]. Additionally, inflammatory responses and fibrotic scarring at the injury site can further impede nerve regeneration [8].

Clinical evaluation of sciatic nerve injuries involves a combination of history-taking, physical examination, and electrodiagnostic studies such as electromyography (EMG) and nerve conduction studies (NCS) [9]. Imaging modalities, including MRI and high-resolution ultrasound, are also increasingly used to assess the extent of nerve damage and guide treatment planning [10]. These diagnostic tools are essential in determining whether surgical intervention is necessary.

The treatment of sciatic nerve injuries is determined by the extent and type of injury. Conservative management, including physical therapy, pain management, and nerve stimulation, is often the first-line approach for mild injuries [11]. However, severe injuries, such as neurotmesis, typically require surgical intervention, including nerve repair, grafting, or nerve transfers [12]. Autologous nerve grafts remain the gold standard for repairing segmental nerve defects, but alternative strategies, such as artificial nerve conduits and stem cell therapies, are being explored [13].

Nerve regeneration after sciatic nerve injury is a slow and complex process. Axonal regrowth occurs at an average rate of 1 mm per day, and functional recovery may take months or even years [14]. Factors such as patient age, comorbidities, and the timing of intervention significantly influence recovery outcomes [15]. Early surgical intervention is generally associated with better functional outcomes.

Neuropathic pain is a common and challenging complication of sciatic nerve injuries. It results from aberrant nerve regeneration and hyperactivity of nociceptive pathways [16]. Pharmacological management, including the use of anticonvulsants (e.g., gabapentin) and antidepressants (e.g., amitriptyline), is commonly employed to address neuropathic pain [17]. In refractory cases, interventions such as spinal cord stimulation may be considered [18].

Functional recovery following sciatic nerve injury is often incomplete, with many patients experiencing residual weakness, sensory deficits, and chronic pain [19]. Rehabilitation plays a critical role in maximizing functional recovery, focusing on muscle strengthening, gait training, and preventing joint contractures [20]. Multidisciplinary care involving physiotherapists, occupational therapists, and pain specialists is essential for optimal outcomes. Research into sciatic nerve injuries is ongoing, with emerging therapies such as stem cell transplantation and growth factor delivery showing promise in preclinical studies [21].

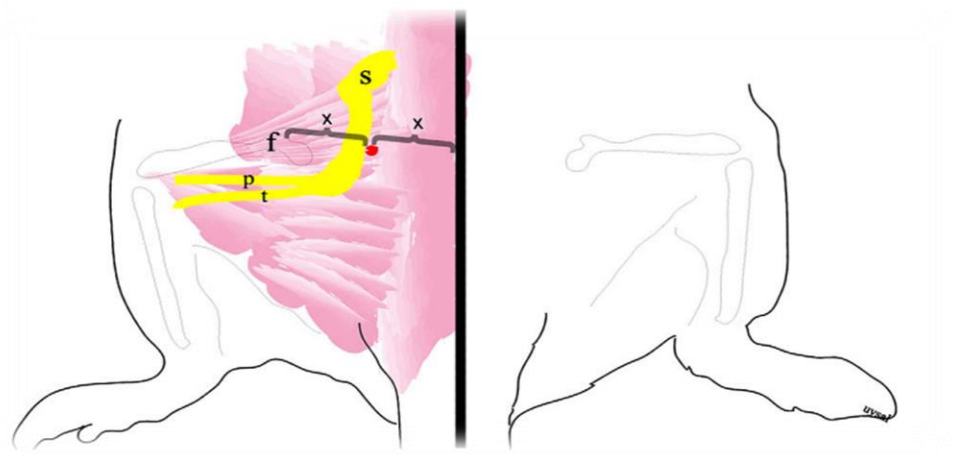

Figure 1:The schematic drawing of the sciatic nerve anatomy in rat. f: femoral head, s: sciatic nerve, p: peroneal nerve, t: tibial nerve. Red dot indicating the skin perforator, which is at the mid-point between the femur head and dorsal midline (Uysal et al., 2009)

Schwann cells, which play a key role in nerve regeneration, are being targeted to enhance axonal growth and functional recovery [22]. Advances in biomaterial engineering have also led to the development of innovative nerve conduits that support axonal regeneration [23].

Biomarkers for nerve injury and regeneration are another area of active research. Serum and tissue biomarkers, including neurofilament light chain and brain-derived neurotrophic factor (BDNF), are being investigated for their potential to predict outcomes and guide treatment decisions [24]. These biomarkers may help in the early identification of patients who are unlikely to recover with conservative management alone.

Patient-reported outcome measures (PROMs) are increasingly being used to assess the impact of sciatic nerve injuries on quality of life [25]. These tools capture patient perspectives on pain, functional ability, and psychological well-being, providing valuable insights into treatment effectiveness [26]. PROMs can also help identify unmet needs and guide rehabilitation strategies.

Preventive measures are essential to reduce the incidence of iatrogenic sciatic nerve injuries. Proper injection techniques, careful positioning during surgical procedures, and surgeon training programs are critical in minimizing risk [27]. Education and awareness among healthcare providers remain key priorities in injury prevention.

The economic burden of sciatic nerve injuries is substantial, with costs associated with medical care, rehabilitation, and lost productivity [28]. Early diagnosis and intervention can reduce healthcare expenditures by minimizing long-term disability and complications [29]. Public health initiatives aimed at injury prevention, particularly in high-risk settings, are equally important, sciatic nerve injuries remain a challenging clinical problem with significant functional and economic implications. Advances in diagnostic techniques, surgical interventions, and regenerative therapies are improving outcomes, but challenges remain. Future research focusing on nerve regeneration, pain management, and personalized therapies will be essential to address unmet needs in this field.

Classifications of nerve injuries

Peripheral nerve injuries pose various challenges to patients, ranging from mild discomfort to life-long impairment. A classification scheme provides a common language for physicians and scientists to effectively discuss nerve pathophysiology (

Table 1). **Seddon** was the first to classify nerve injuries into three categories based on the presence of demyelination and the extent of damage to the axons and the connective tissues of the nerve [30].

The mildest form of injury is called neurapraxia, defined by focal demyelination without damage to the axons or the connective tissues. **Neurapraxia** typically occurs from mild compression or traction of the nerve and results in a decrease in conduction velocity. Depending on the severity of demyelination, the effects can range from asynchronous conduction to conduction block, causing muscle weakness. The next level is called **Axonotmesis**, which involves direct damage to the axons in addition to focal demyelination while maintaining continuity of the nerve's connective tissues. The most severe form of injury is called **Neurotmesis**, which is a full transection of the axons and connective tissue layers wherein complete discontinuity of the nerve is observed [30].

Table 1: Seddon and Sunderland Classification of Nerve Injury

Seddon	Sunderland	Injury
Neurapraxia	Grade I	Focal segmental demyelination
Axonotmesis	Grade II	Axon damaged with intact endoneurium
Axonotmesis	Grade III	Axon and endoneurium damaged with intact perineurium
Axonotmesis	Grade IV	Axon, endoneurium, and perineurium damaged with intact epineurium
Neurotmesis	Grade V	Complete nerve transection.
	Grade VI (MacKinnon & Dellon)	Mixed levels of injury along the nerve

Sunderland later expanded on this classification to distinguish the extent of damage in the connective tissues in his classification scheme, Grade I and Grade V corresponded with Seddon's neurapraxia and neurotmesis respectively. However, Grade II-IV are all forms of axonotmesis with increasing amounts of connective tissue damage. In Grade II, axon damage is observed with no damage present in the connective tissue. Grade III involves damage to the endoneurium and Grade IV includes damage to the perineurium. A Grade VI lesion was later introduced nerve,althoughits usage has not been widelyaccepted[30]. by **McKennon and Dellon** to denote combinations of Grade III-V injuries along a damaged

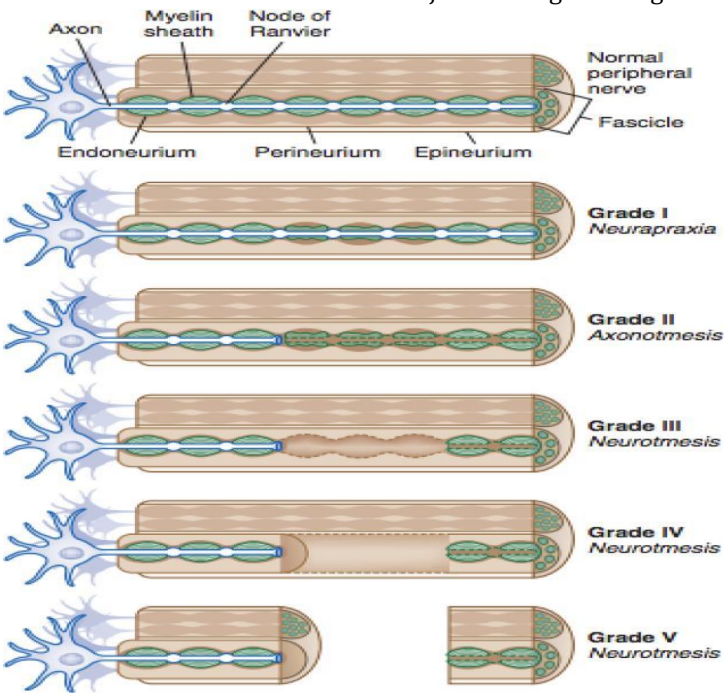

Figure 2: Classification of nerve trauma [30].

Open versus closed injuries

Nerve injuries can be classified as closed and open depending on whether the cutaneous integrity has been disrupted or not. Closed injuries are more frequently associated with nerve injuries in continuity, characterized by absence of nerve rupture and by occurrence of neuropraxis and axonotmesis as the predominant mechanisms of injury. Therefore, spontaneous recovery is possible and surgery is indicated only after 3 months if no recovery is identified. This period is arbitrated based on axonal growth rate (1–3 mm/day) and improvement identified on clinical or electromyographic evaluation. Classical examples of closed injuries are those resulting from stretching after brachial plexus injuries secondary to motorcycle falls and peroneal nerve injuries associated with knee dislocation and concomitant ligament lesion. Conversely, the occurrence of an open injury related to a nerve course has been more frequently related to neurotmetic injuries and must be treated with early surgery. Examples of these injuries include those provoked by knives, propellers, piece of glass, and scalpel iatrogenic lesions. Within this context, it is important to keep in mind that the distal portion of the nerve undergoes Wallerian degeneration that occurs up 2 to 3 weeks after the injury. So, electrophysiological assessment is not indicated in these cases before 3–4 weeks, since false results may compromise the evaluation [31].

Sharp versus blunt injuries

The aspect of the nerve stumps identified during surgery is another important factor to be considered for the definitive treatment. Two situations can be distinguished: identification of a sharp stump with homogeneous aspect and no significant inflammation; or finding a blunt or rugged stump, associated with significant inflammatory process, heterogeneous aspect, and contusion. Sharp instruments like knives or scalpels have been identified as a frequent causative factor resulting in sharp stumps. In these cases, the repair should be done promptly, if possible, within the first 3 days after the injury. Usually, a direct coaptation of the nerve ends can be performed with a termino-terminal tension-free suture. Technical conditions in performing surgery are another important issue that must be taken into consideration when deciding on an early repair, as an adequate surgical technique has been accepted as one of the factors that influence the final result after a nerve surgery. This implies the use of microscope magnification, 9.0- or 10.0-caliber sutures, and a careful manipulation of nerve structures using microsurgical instrumental [31].

If there are no such conditions for surgery, the epineurium of each nerve stump should be sutured to some adjacent structure, such as a tendon or fascia, in order to avoid excessive retraction of the stumps and to facilitate its identification in a second surgical procedure. Any attempt to suture the nerve beyond these conditions will result in unnecessary damage to nerve tissue, increase in local fibrosis, and worse functional results at long-term follow-up. When blunt stumps are identified during surgery, the repair should not be performed immediately because the inflammatory process that takes place extends for up to 3 weeks after the injury. If repair is performed within this period there is a risk to connect nerve stumps still involved in an ongoing inflammatory process that results in fibrosis and prevents progression of the regenerated axons. When blunt nerve stumps are identified, the surgeon should interrupt the procedure and perform the definitive repair 3 weeks after the injury. During the definitive repair the inflammatory tissue and fibrosis must be resected by trimming the nerve ends with a scalpel blade until viable fascicles have being exposed [31].

Autogenous Fat Grafting and Platelet Rich Plasma (PRP) in Sciatic Nerve Graft Regeneration

Autogenous fat grafting and platelet-rich plasma (PRP) have emerged as promising strategies in the field of peripheral nerve regeneration, specifically for sciatic nerve injuries. Sciatic nerve injuries are debilitating, often resulting in sensory and motor deficits that significantly affect the quality of life [30]. Despite advancements in microsurgical techniques, functional recovery remains suboptimal in many cases, driving interest in adjunct therapies such as fat grafts and PRP [31].

Fat grafting has been widely utilized in reconstructive surgery due to its biocompatibility, abundance, and potential for regenerative properties [32]. Autogenous fat, harvested typically from the abdominal or gluteal region, contains adipose-derived stem cells (ASCs) capable of differentiating into neuronal and Schwann-like cells, which play critical roles in nerve regeneration [33]. Furthermore, the extracellular matrix (ECM) within fat grafts provides a supportive microenvironment for axonal growth [34].

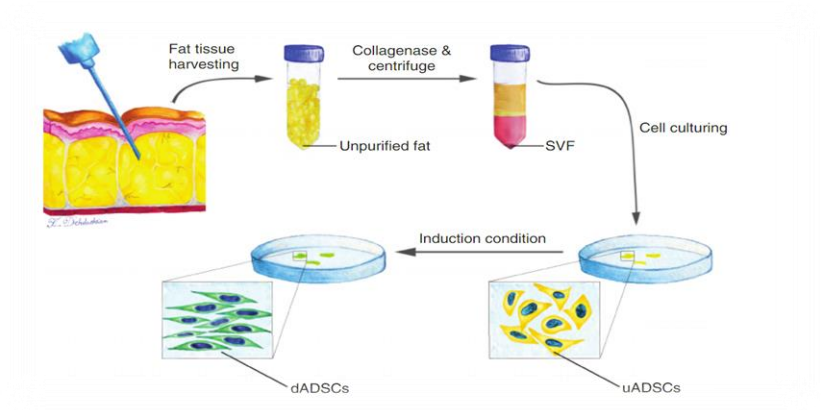

Figure 3: Subcutaneous adipose tissue is a rich source of adipose-derived stem cells that is easily accessible to harvest. Unpurified fat is used routinely in reconstructive surgeries. SVF is a concentrated product of ADSCs, which is obtained through collagenase digestion followed by centrifugation. Resuspension of SVF and then cell culture isolates purified uADSCs. Specific culture media can be used to induce phenotype changes toward Schwann cell dADSCs (Dehdashtian et al., 2020).

Platelet-rich plasma (PRP), derived from autologous blood, is rich in growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), and vascular endothelial growth factor (VEGF) [35]. These bioactive molecules are essential for cell proliferation, angiogenesis, and extracellular matrix remodeling, which collectively contribute to nerve repair [36]. PRP has been shown to enhance Schwann cell proliferation and migration, creating an optimal milieu for nerve regeneration [37].

The synergistic effect of autogenous fat grafting and PRP has been hypothesized to optimize the regenerative process in sciatic nerve injuries. Fat grafts offer structural support and cellular components, while PRP provides a biochemical boost, enhancing cellular activity and angiogenesis [38]. This combined approach holds promise for improving functional outcomes compared to traditional nerve grafting alone [39].

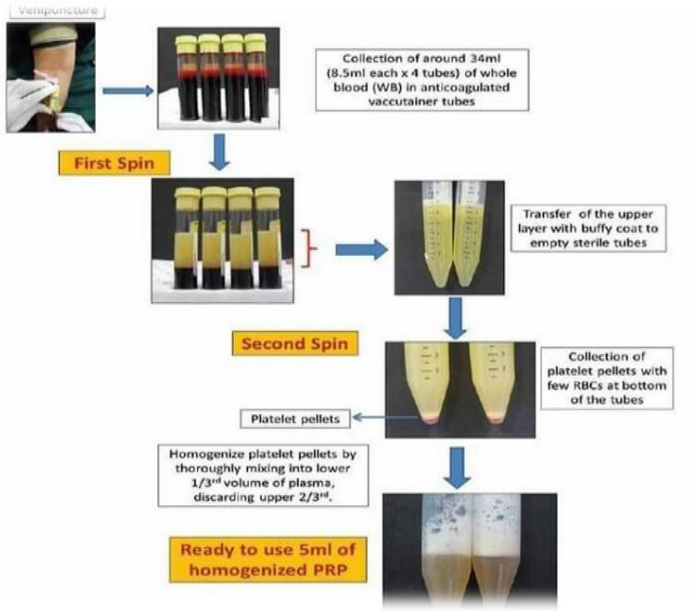

Fig. (15): Flow chart describes a double centrifugation process of PRP. (Dhurat & Sukesh, 2015)

One of the key advantages of autogenous fat grafting is its availability and minimal immunogenicity, reducing the risk of rejection or adverse inflammatory reactions [40]. Furthermore, the ease of harvesting and processing makes it a practical option in clinical settings [41]. Studies have demonstrated that adipose-derived stem cells (ADSCs) can enhance axonal regeneration by modulating the inflammatory response and secreting neurotrophic factors [42].

PRP, on the other hand, offers a concentration of growth factors essential for tissue healing and regeneration. Its application in sciatic nerve repair has demonstrated increased axonal growth, improved remyelination, and enhanced motor function recovery in preclinical models [43]. PRP's ability to reduce oxidative stress and inflammation further supports its role in promoting nerve healing [44].

Experimental studies using sciatic nerve injury models have shown encouraging results with the combination of autogenous fat grafting and PRP. In a rat sciatic nerve transection model, animals treated with fat grafts enriched with PRP exhibited superior nerve conduction velocities and histological recovery compared to controls [45]. This highlights the potential clinical translation of these findings into human therapies [46].

Despite these promising results, several challenges remain in optimizing the clinical use of fat grafts and PRP in nerve repair. One of the major concerns is the variability in PRP preparation protocols, which can lead to inconsistent outcomes [47]. Standardization of PRP processing and application techniques is essential for reproducibility and efficacy [48].

Fat graft survival is another critical factor influencing outcomes. Graft resorption and fibrosis over time can compromise the long-term benefits of the treatment [49]. Techniques such as centrifugation, enzymatic digestion, and decellularization have been explored to improve fat graft stability and integration into nerve grafts [50].

Recent advances in tissue engineering have led to the development of composite grafts, combining fat tissue, PRP, and bioengineered scaffolds. These constructs aim to provide both structural and biochemical support for

nerve regeneration [51]. Hydrogel-based scaffolds infused with PRP and ADSCs have shown promise in enhancing nerve repair outcomes in animal models [52].

In terms of clinical applications, several case reports and small-scale studies have demonstrated the safety and efficacy of autogenous fat grafts and PRP in treating peripheral nerve injuries [53]. However, large-scale randomized controlled trials (RCTs) are still lacking, highlighting the need for further research to establish evidence-based protocols [54].
Moreover, the timing of PRP and fat graft application in the nerve repair process remains a subject of debate. Some studies suggest that early intervention yields better results, while others propose delayed application after initial nerve repair [55]. Understanding the optimal timing and sequence of these interventions is crucial for maximizing their therapeutic potential [56].

In terms of cellular mechanisms, ADSCs derived from autogenous fat have been shown to secrete exosomes containing microRNAs and growth factors that modulate Schwann cell activity and axonal growth [57]. These paracrine signaling pathways are thought to play a significant role in the regenerative effects observed with fat grafts and PRP [58].
Furthermore, PRP has been shown to reduce scar tissue formation at the injury site, thereby minimizing physical barriers to axonal regeneration [59]. The anti-inflammatory properties of PRP, mediated by cytokines and growth factors, further support its role in nerve healing [60].
Clinically, autogenous fat grafting and PRP have been used as adjuncts in nerve repair procedures, particularly in complex injuries where nerve gaps exceed the limits of direct repair [61]. Their use in combination with autologous nerve grafts or conduits has been explored with promising outcomes [62].

Patient-reported outcomes and functional assessments have shown improvements in sensory and motor recovery following treatment with fat grafts and PRP [63]. Electrophysiological studies have also demonstrated enhanced nerve conduction velocities in treated patients [64].
In conclusion, autogenous fat grafting and PRP represent promising adjunct therapies in sciatic nerve graft regeneration. Their combined use offers structural support, cellular components, and biochemical signals necessary for optimal nerve repair [65]. Further research, including well-designed clinical trials, is needed to validate these findings and establish standardized protocols for their clinical application [66].

Sciatic nerve injuries are among the most debilitating peripheral nerve injuries, often resulting from trauma, compression, or iatrogenic causes. These injuries can lead to significant motor and sensory deficits, including foot drop, muscle atrophy, and chronic neuropathic pain. The sciatic nerve, being the largest nerve in the body, plays a crucial role in lower limb function, making its repair a priority in clinical practice. Despite advances in microsurgical techniques, functional recovery remains suboptimal, necessitating innovative approaches such as autogenous fat grafting and platelet-rich plasma (PRP) to enhance regeneration [67].

Autogenous Fat Grafting versus Platelet-Rich Plasma (PRP) in Sciatic Nerve Graft Regeneration

Introduction to Sciatic Nerve Injuries and Regeneration Challenges

Sciatic nerve injuries are among the most debilitating peripheral nerve injuries, often resulting from trauma, compression, or iatrogenic causes. These injuries can lead to significant motor and sensory deficits, including foot drop, muscle atrophy, and chronic neuropathic pain. The sciatic nerve, being the largest nerve in the body, plays a crucial role in lower limb function, making its repair a priority in clinical practice. Despite advances in microsurgical techniques, functional recovery remains suboptimal, necessitating innovative approaches such as autogenous fat grafting and platelet-rich plasma (PRP) to enhance regeneration [67].

Autogenous Fat Grafting: Mechanism and Application

Autogenous fat grafting involves the transplantation of adipose tissue from a donor site to the injured nerve area. This technique leverages the regenerative potential of adipose-derived stem cells (ADSCs) present in the fat graft. ADSCs secrete neurotrophic factors, such as nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF), which promote axonal regeneration and Schwann cell proliferation. Additionally, the fat graft provides a physical barrier against scar tissue formation, reducing perineural adhesions and improving the microenvironment for nerve repair [68].

Platelet-Rich Plasma (PRP): Composition and Role in Nerve Regeneration

PRP is a concentrated plasma fraction rich in growth factors, including platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and transforming growth factor-beta (TGF-β). These factors play a pivotal role in angiogenesis, inflammation modulation, and axonal sprouting. PRP can be injected into the nerve graft site or combined with other biomaterials, such as chitin conduits, to enhance nerve regeneration. Its gel-like consistency also provides structural support, mimicking the extracellular matrix and facilitating axonal growth [69].

Comparison of Mechanisms: Autogenous Fat Grafting vs. PRP

While both autogenous fat grafting and PRP aim to enhance nerve regeneration, their mechanisms differ significantly. Fat grafting primarily relies on the regenerative potential of ADSCs and their paracrine effects, whereas PRP focuses on delivering a high concentration of growth factors to the injury site. Fat grafting provides a structural barrier against scar tissue, while PRP promotes angiogenesis and axonal sprouting. These differences make each technique suitable for specific clinical scenarios, depending on the nature and severity of the nerve injury [70].

Advantages of Autogenous Fat Grafting

One of the primary advantages of autogenous fat grafting is its autologous nature, minimizing the risk of immune rejection. The procedure is minimally invasive and can be performed using liposuction techniques, making it readily available for clinical use. Additionally, the ADSCs in the fat graft have multipotent differentiation potential, contributing to tissue repair beyond nerve regeneration. The fat graft also provides a physical barrier against scar tissue, improving the microenvironment for nerve repair [71].

Disadvantages of Autogenous Fat Grafting

Despite its advantages, autogenous fat grafting has limitations. The variability in the quality and quantity of ADSCs can affect outcomes, and the procedure requires specialized skills for fat harvesting and processing. Long-term studies are needed to assess the durability of functional recovery and the risk of complications, such as fat necrosis or graft resorption. Additionally, the procedure may not be suitable for patients with limited adipose tissue availability [72].

Advantages of PRP

PRP offers several advantages, including its autologous nature and high concentration of growth factors. The procedure is minimally invasive and can be prepared quickly using the patient's blood. PRP promotes angiogenesis, reduces inflammation, and enhances axonal sprouting, making it a versatile tool for nerve regeneration. Its gel-like consistency also provides structural support, mimicking the extracellular matrix and facilitating axonal growth [73].

Disadvantages of PRP

The primary disadvantage of PRP is the variability in growth factor concentration, which can affect outcomes. The procedure requires specialized equipment for blood processing, which may not be available in all clinical settings. Additionally, the effects of PRP are often short-lived, necessitating repeated applications in some cases. Long-term studies are needed to evaluate the safety and efficacy of PRP in nerve regeneration [74].

Preclinical Evidence Supporting Autogenous Fat Grafting

Preclinical studies have demonstrated the efficacy of autogenous fat grafting in nerve regeneration. For example, studies using rat models of sciatic nerve injury have shown improved axonal growth, myelination,

and functional recovery with fat grafting. The ADSCs in the fat graft secrete neurotrophic factors and reduce scar tissue formation, creating a conducive environment for nerve repair [75].

Preclinical Evidence Supporting PRP

PRP has also shown promising results in preclinical studies. For instance, studies using rat models of sciatic nerve injury have demonstrated enhanced axonal regeneration, angiogenesis, and functional recovery with PRP. The growth factors in PRP promote Schwann cell proliferation and axonal sprouting, making it a valuable tool for nerve repair [76].

Clinical Applications of Autogenous Fat Grafting

Autogenous fat grafting has been used in clinical settings to prevent perineural adhesions and improve nerve regeneration. For example, fat grafting has been employed in patients undergoing peripheral nerve surgery, with reports of reduced scar tissue formation and improved functional outcomes. These findings suggest that fat grafting is a viable option for clinical use [77].

Clinical Applications of PRP

PRP has been employed in nerve repair surgeries, with reports of reduced neuropathic pain and improved sensory recovery. For instance, PRP has been used in patients with carpal tunnel syndrome and sciatic nerve injuries, demonstrating its potential for enhancing nerve regeneration. These findings highlight the versatility of PRP in clinical applications [78].

Combination of Autogenous Fat Grafting and PRP

The synergistic use of autogenous fat grafting and PRP has shown promising results in preclinical studies. The ADSCs in the fat graft complement the growth factors in PRP, creating a conducive environment for nerve regeneration. For example, studies have demonstrated improved axonal growth, myelination, and functional recovery in rat models of sciatic nerve injury when these two therapies are combined [79].

Role of Biomaterials in Enhancing Nerve Regeneration

Biomaterials, such as chitin conduits and polyglycolic acid (PGA) meshes, can further enhance the efficacy of autogenous fat grafting and PRP. These materials provide a scaffold for axonal growth and can be loaded with ADSCs and PRP to create a bioactive nerve graft. For example, a study using a PGA-PRL mesh combined with ADSCs and PRP demonstrated significant improvements in nerve regeneration and functional recovery in a canine model of sciatic nerve injury [80].

Challenges in Clinical Translation

Translating these therapies from preclinical models to clinical practice poses several challenges. Standardizing the preparation and application of fat grafts and PRP is crucial to ensure consistent outcomes. Regulatory hurdles, particularly for PRP-based therapies, also need to be addressed. Additionally, long-term follow-up studies are required to evaluate the safety and efficacy of these approaches in human patients [81].

Future Directions and Research Opportunities

Future research should focus on optimizing the combination of autogenous fat grafting and PRP, exploring novel biomaterials, and developing standardized protocols for clinical use. Advances in tissue engineering, such as 3D-printed nerve conduits and gene-edited stem cells, could further enhance the regenerative potential of these therapies. Collaborative efforts between researchers, clinicians, and regulatory bodies are essential to overcome existing challenges and bring these therapies to patients [82].

Economic and Ethical Considerations

The cost-effectiveness of autogenous fat grafting and PRP makes them attractive options for nerve repair, particularly in resource-limited settings. However, ethical considerations, such as the sourcing of adipose tissue and the potential for commercialization, must be addressed. Ensuring equitable access to these therapies and maintaining ethical standards in their application are critical for their widespread adoption [83].

Patient Selection and Personalized Therapy

Patient selection is a key factor in the success of these therapies. Factors such as age, comorbidities, and the extent of nerve injury should be considered when determining eligibility. Personalized therapy, tailored to the patient's specific needs, could further improve outcomes. For example, patients with severe nerve injuries may

benefit from higher concentrations of ADSCs and PRP, while those with mild injuries may require less intensive treatment [84].

Integration with Rehabilitation Programs

Rehabilitation plays a crucial role in maximizing functional recovery after nerve repair. Physical therapy, occupational therapy, and pain management should be integrated with autogenous fat grafting and PRP to optimize outcomes. Early intervention and a multidisciplinary approach are essential to address the complex needs of patients with sciatic nerve injuries [85].

Conclusion

Autogenous fat grafting and PRP represent promising approaches for sciatic nerve graft regeneration. While each technique has its advantages and disadvantages, their combined use offers synergistic benefits for nerve repair. Preclinical studies have shown encouraging results, but further research is needed to overcome existing limitations and translate these therapies into clinical practice. With continued innovation and collaboration, these therapies could revolutionize the treatment of peripheral nerve injuries [86].

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