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Short Communication

Fat as an Adjunct in Nerve Surgery

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Peripheral nerve surgery involves suturing an injured nerve to itself or to another nerve end-to-end or side-to-end to promote regeneration of the damaged nerve. Nerve surgeries include repair, grafting, transfer, and decompression. Poor outcomes of nerve surgery can occur if the nerve incompletely heals, which can result in motor and/or sensory deficits depending on the type of nerve. Adipose tissue has been exploratively used as an adjunct to peripheral nerve surgery in an attempt to provide additional support to repaired nerves and promote the healing process.

Adipose tissue contains Adipose-Derived Stem Cells (ADSCs), which supply the regenerative properties of the tissue. ADSCs can produce exosomes occupied with transcripts for various neural growth factors to aid in Schwann cell proliferation and, ultimately, axon regrowth [1]. Stem cells in adipose tissue have demonstrated ability to express Brain-Derived Neurotrophic Factor (BDNF), Glial-Derived Neurotrophic Factor (GDNF), Ciliary Neurotrophic Factor (CNTF), basic Fibroblasts Growth Factor (bFGF), insulin-like growth factor 1 (IGF-1), Nerve Growth Factor (NGF) and neutrophin-3 and -4 (NT-3, NT-4) which correlated with increases in axon sprouting [2]. In vivo, ADSCs exhibit migration to sites distal to the injury, which is where Wallerian degeneration and subsequent axon regrowth occur [3]. Schwann cells are responsible for myelination in the peripheral nervous system. ADSCs present in adipose tissue have been shown to support existing Schwann cells at the site of injury, as well as possess the ability to differentiate into Schwann-like cells themselves [4,5]. Additionally, fat grafting after sciatic nerve surgery in rats resulted in decreased scar tissue growth [6]. Adhesions around the site of surgical nerve repair can lead to worse outcomes by restricting free movement, so minimizing scar tissue is an added benefit provided by ADSCs.

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In a recent review, our group explored the literature regarding the use of adipose tissue and ADSCs in conjunction with peripheral nerve surgeries in animal studies [7]. Studies of surgical repairs, grafts, Tissue-Engineered Nerve Grafts (TENGs), and transfers that used fat grafting or ADSC injection near the site of repair were evaluated. Some of the most compelling nerve repair studies showed improved functional recovery on a swim test at 2 and 6 weeks with ADSC injection near the repair site and increased functional recovery determined by pin prick test after fat grafting [8,9]. Nerve grafting animal studies with ADSC supplementation obtained results revealing more myelin fibers, increased distal muscle responsiveness on electromyography, and reduced reinnervation time compared to controls [10,11]. Numerous experiments utilizing ADSCs with TENGs had positive results, but all studies had small sample sizes with the largest sample size being n=16. Notably, nerve transfers in conjunction with ADSCs correlated functional outcomes with histological results, which provides a more powerful level of evidence. Abbas et al. correlated vibrissae motor performances with histological results of facial nerve transfers with and without ADSCs [12]. Additionally, Yang et al., correlated modified grooming test results to evaluate various shoulder movements and elbow flexion with histological results of brachial plexus C7 nerve transfers with and without ADSC seeding in engineered nerve grafts [13]. Animal studies provide insight to the mechanisms of action of the ADSCs in adipose tissue on damaged and regenerating peripheral nerves on a level that is not always attainable or ethical in human studies.

Though more animal studies exist, a small number of human studies concerning the use of fat grafting concomitant with peripheral nerve surgery are present in the literature. Of the types of peripheral nerve surgery, use of fat grafting with nerve release for decompression surgery seems the most explored, likely exploiting the ability of adipose tissue to reduce scar tissue formation. A retrospective study of 40 patients regarding the use of free fat grafts in secondary surgical decompression of recalcitrant carpal tunnel syndrome concluded there to be no benefit of fat grafted groups compared to controls [14]. Fat grafted patients reported more scar sensitivity immediately after surgery, but long term follow up revealed no difference in scar sensitivity between fat grafted patients and controls. A study of three patients undergoing secondary decompression of median or ulnar nerves with ADSC injection noted gradual sensory recovery at 36 months with no reported adverse effects [15]. Though promising results were obtained, the study would hold more power if ADSC supplemented patient results were compared to control patient results.

Peripheral nerve injuries present challenges in healing even after surgical correction and can prove disabling [16]. Novel ideas about how to improve nerve surgery outcomes are becoming increasingly explored. ADSCs present in adipose tissue have shown promising regenerative properties on peripheral nerves and the nerve microenvironment in vitro, in animal experiments, and in some human studies. For now, animal studies correlating functional outcomes with histological observations provide the most powerful and convincing evidence for the use of fat in conjunction with peripheral nerve surgery. More human studies, especially randomized control trials, will need to be performed to draw conclusions on the usefulness of fat grafting as an adjunct to peripheral nerve surgery in humans.

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