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End-to-side neurorrhaphy using an electrospun PCL/collagen nerve conduit for complex peripheral motor nerve regeneration

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ABSTRACT

In cases of complex neuromuscular defects, finding the proximal stump of a transected nerve in order to restore innervation to damaged muscle is often impossible. In this study we investigated whether a neighboring uninjured nerve could serve as a source of innervation of denervated damaged muscle through a biomaterial-based nerve conduit while preserving the uninjured nerve function. Tubular nerve conduits were fabricated by electrospinning a polymer blend consisting of poly(ε-caprolactone) (PCL) and type I collagen. Using a rat model of common peroneal injury, the proximal end of the nerve conduit was connected to the side of the adjacent uninjured tibial branch (TB) of the sciatic nerve after partial axotomy, and the distal end of the conduit was connected to the distal stump of the common peroneal nerve (CPN). The axonal continuity recovered through the nerve conduit at 8 weeks after surgery. Recovery of denervated muscle function was achieved, and simultaneously, the donor muscle, which was innervated by the axotomized TB also recovered at 20 weeks after surgery. Therefore, this end-to-side neurorrhaphy (ETS) technique using the electrospun PCL/collagen conduit appears to be clinically feasible and would be a useful alternative in instances where autologous nerve grafts or an adequate proximal nerve stump is unavailable.

1. Introduction

Muscle denervation can cause permanent muscular atrophy and eventual functional disability. Coaptation of transected nerves is critical in avoiding these problems [1]. In cases of complex neuromuscular defects created by gunshot wounds or malignant tumors, finding the proximal stump of a transected nerve for use in coaptation is often impossible [2]. In these circumstances, end-to-side neurorrhaphy (ETS) using an adjacent uninjured nerve (with or without an autologous nerve graft) can be used as an alternative method to reinnervate the denervated muscle. ETS was originally introduced as early as 1903 for facial nerve reconstruction using the spinal accessory nerve as a donor source [2,3]. This technique was reintroduced in 1994 and has been used in clinical and experimental practices for nerve repair cases [2,3]. In ETS, the distal nerve stump, termed as the "recipient nerve", is coapted to the sidewall of an uninjured nerve, termed as the "donor nerve" [3,4]. Theoretically, axonal regeneration in the ETS model, which occurs through collateral sprouting, originates in the donor nerve and progresses towards the recipient stump. This may allow muscle reinnervation while preserving the donor nerve function, and is particularly useful when the proximal stump of an injured nerve cannot be found [3,5]. Consequently, an autologous nerve graft is usually used as a standard procedure in ETS cases to repair the gap between the donor and the recipient nerves. However, excessive tension on the nerve frequently results in impaired microvascular flow in the nerve tissue and excessive scarring at the repair site [6–8]. This is especially true for grafts other than autologous donor nerve.

Despite a long history and high demand for this technique, clinical application of ETS is still limited and even controversial. This is mainly due to the less likelihood of sidewall donor axonal sprouting to the recipient nerve and possible donor muscle damage following donor nerve axotomy. From a clinical point of view, these problems often escalate when an autologous nerve graft is used due

Abbreviations: ETS, end-to-side neurorrhaphy; ETE, end-to-end neurorraphy; NGC, nerve guidance channel; NR, non repair group; ETSC, repair group with ETS and a conduit; AchR, acetylcholine receptor; CMAP, compound muscle action potential; EMG, electromyogram; GA, gastrocnemius muscle; AT, anterior tibialis muscle; EDL, extensor digitorium longus muscle; NMJ, neuromuscular junction.

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