Neural Reanimation Advances and New Technologies

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KEYWORDS

• Facial reanimation • Nerve substitution • Hypoglossal nerve transfer • Masseteric nerve transfer • Facial nerve regeneration • Nerve conduit • Facial paralysis treatment

KEY POINTS

- Review of peripheral nerve anatomy, injury, and repair.
- The goal of facial reanimation is to restore facial symmetry and function by primary nerve repair whenever possible, followed by nerve substitution.
- There is an explosion of applicable technology related to biomedical and tissue engineering toward facial reanimation.

Videos of patients after neural reanimation surgery accompany this article at http://www.facialplastic.theclinics.com/

There is no treatment that can guarantee total recovery and normalization of function following repair of an injured nerve. The poor outcome reflects the complexity of peripheral nerve injuries and the diversity of cellular and biochemical events required to regain function. Facial reanimation has been an area of much research by surgeons, research scientists, biomedical engineers, and tissue engineers due to the devastating impact of facial paralysis aesthetically and functionally. This article focuses on advances in neural reanimation as well as new technologies on the horizon.

This will include discussion of nerve repair, cable grafting, nerve substitution procedures, use of conduits, autografts and allografts, and future directions.

NERVE INJURY

It is important to review the process of nerve injury and repair when considering therapeutic strategies to simultaneously potentiate axonal regeneration, neuronal survival, modulate central reorganization, and inhibit target organ atrophy. The processes of nerve regeneration and target reinnervation are complex, involving physiologic, biochemical, and cellular changes throughout the whole length of the neuron.[1]

From the moment of injury, the distal nerve stump undergoes Wallerian degeneration, while the proximal stump retracts and the Schwann cells activate nearby macrophages to clear the injured axon.[2]

In addition to debris removal, Schwann cells serve several other functions important for recovery from nerve damage. Whereas these cells normally provide axonal myelin to enhance action potential conduction speed, axon transection causes Schwann cells in the distal end of the transected nerve to switch from a myelination phenotype to a growth-supportive one.[3]

The axon sprouts and a growth cone is formed at the tip of each sprout, interacting with activated and proliferating Schwann cells.[4]

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Changes also occur to the proximal neuronal cell bodies in dorsal root ganglia with a shift in protein synthesis from a "signaling mode" to a "growing mode" and protein synthesis switches from neurotransmitter-related substances to those required for axonal reconstruction.[5] The gap at the injury site is aligned by Schwann cells coming from the distal stump to form columns of cells called the bands of Bungner.[6] These columns act as a natural "conduit" to guide and help the regenerating axons reach the end organ. Dedifferentiated Schwann cells upregulate the expression of many regeneration-related elements, such as laminin and collagen, which make up the vital extracellular matrix of the nerve.[7] Regeneration involves contact guidance between the growing axon tip and the Schwann cells lining the tube. The regenerated axon must reinnervate the proper target, and the target must retain the ability to accept reinnervation and recover from denervation-related atrophy.[7] Regeneration rate is approximately 1 mm per day; therefore, more proximal injuries lead to longer denervation periods.[8]

Understanding the complex process of regeneration has spurred research in tissue engineering of natural and artificial conduits and the emerging role of cell-based supportive therapies in nerve repair.[9–12]

NERVE ANATOMY

It is also important to understand the structural anatomy of the nerve, which includes mesoneurium, epineurium, perineurium, and endoneurium.[13] The mesoneurium is a connective tissue sheath that suspends the nerve trunk within the soft tissue that contains the segmental blood supply to the nerve. The epineurium is a layer of loose scattered fibroblasts, and adipocytes that defines the nerve trunk and provides mechanical protection. Within the nerve trunk, the perineurium is a multilayered sheath of flattened and densely packed supporting pericytes that surrounds groups of axons, and subdivides the nerve into fascicular bundles. Additionally, the perineurium is the major contributor to nerve tensile strength, serves as a diffusion barrier analogous to the blood-nerve barrier, and contains a latticework for vascular bed. The endoneurium is a loose collagenous matrix within each nerve fascicle that surrounds the individual axons and their Schwann cells (**Fig. 1**).

The blood supply to the peripheral nerve is a complex vascular plexus fed by radicular vessels in the mesoneurium. Anastomotic connections between epineurial and perineurial plexi occur at

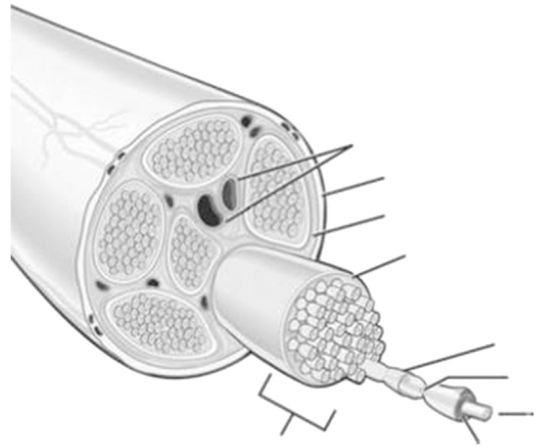

Fig. 1. Schematic presentation of peripheral nerve anatomy. A peripheral nerve is composed of axons of multiple neurons bundled in connective tissue fascicles surrounded by perineurium. Within the nerve, microvasculature runs along the outer layer (epineurium) with a transverse capillary network perfusing the endoneurium. Each fascile itself is composed of endoneurium containing multiple neurons surrounded with myelin produced by Schwann cells. (*From* Siemionow M, Brzezicki G. Current techniques and concepts in peripheral nerve repair. Int Rev Neurobiol 2009;87:143; with permission.)

various levels in the perineurium and eventually arborize into the network of endoneurial capillaries. This vascular plexus is exquisitely sensitive to tension, as animal studies have demonstrated an 80% decrease in blood flow and irreversible ischemic damage with a 15% increase in nerve tension.[14]

Hence, the development of cable grafts and conduits to provide tension-free coaptation and intact vascularity for successful regeneration. It is important to realize and educate the patient that the preinjury facial form and function is never attainable.

NERVE REPAIR

There are 3 surgical reconstruction strategies: (1) direct repair, in which the proximal and distal nerve ends are sutured back together; (2) nerve grafting, required to bridge a gap between nerve ends; and (3) nerve transfer, when the distal or proximal nerve segment is unusable or missing.

Primary Suture Repair

The basic principles of facial nerve repair have changed little since Bunnell performed the first successful infratemporal coaptation in the late 1920s.[15] Primary tension-free neurorrhaphy of