Functional Recovery of Completely Denervated Muscle by Direct Nerve Transplantation

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Introduction

To engineer functional muscle tissue for reconstruction, integration of nerve is necessary. It is uncertain whether implantation of engineered muscle constructs, which is analogous to denervated muscle, could be innervated when native nervous tissue were provided. In this study we investigated whether transplantation of native nerve into complete denervated muscle (neurotization) would lead to functional recovery and form neuromuscular junction.

Methods

Eighty Lewis rats were divided into three groups: a normal control group (n=16); a denervated group (n=32); and a transplantation group muscle (n=32). Denervation was achieved by removing a 10mm segment of the sciatic nerve including the common peroneal nerve, tibial nerve and sensory nerve branch. Direct nerve transplantation was achieved by embedding the common peroneal nerve into the gastrocnemius muscle after excision of tibial nerve and sensory nerve branch. Neurofunctional behavior including extensor postural thrust (EPT) and withdrawal reflex latency (WRL), compound muscle action potential (CMAP), and histological evaluations using alpha-bungarotoxin and anti-NF-200, were performed at 2, 4, 8 and 12 weeks (n=8) after surgery.

- Denervation: Excision of all branches of sciatic nerve (CPN, TN, SB)
- Neurotization: Transplantation of CPN into gastrocnemeus muscle (GM)

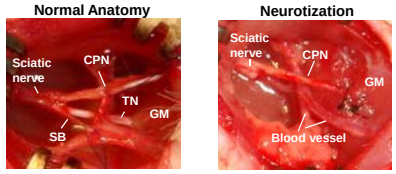

Figure. 1. Surgical procedure of denervation and neurotization in a rat model.

Results

EPT and WRL were improved in the transplantation group compared to the denervated group, but the levels were significantly lower than the normal control group, even at 12 weeks (EPT, 26.3±13.8 vs 155.0±38.9 g, $P < 0.001$; WRL, 8.3±5.5 vs 2.7±2.30 sec, $P = 0.027$). CMAP latency and amplitude significantly improved in the transplantation group with time ($P < 0.001$, one-way ANOVA), and at 12 weeks was not statistically different from the normal control group (latency, 0.9±0.0 vs 1.3±0.7 sec, $P = 0.164$; amplitude, 30.2±7.0 vs 46.4±26.9 mV, $P = 0.184$). Recovery of the neuromuscular junction was demonstrated histologically in the transplantation group.

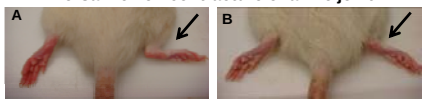

Figure 2. Neurobehavior study: posture of leg of (A) control and (B) neurotization groups.

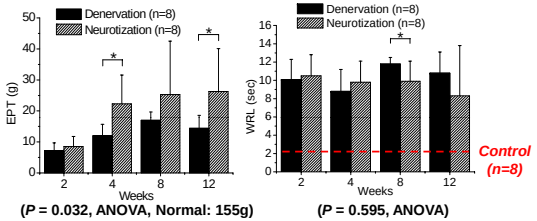

Figure 3. Neurobehavior study: (A) extensor postural thrust motor and (B) withdrawal reflex latency sensory.

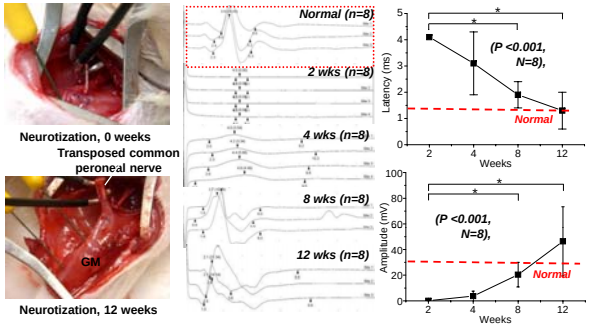

Figure 4. Electrophysiologic study : Experimental groups after neurotization for the evaluation of muscle function recovery.

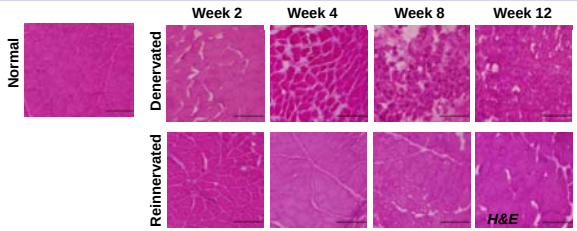

Figure 5. Histological evaluation of reinnervation of denervated gastrocnemius muscle.

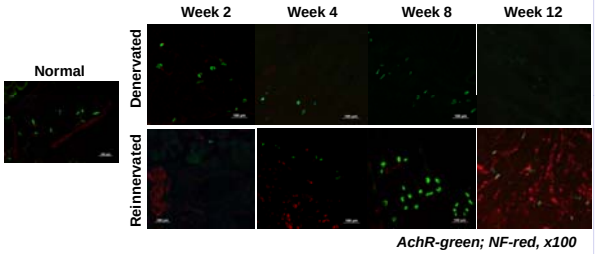

Figure 6. Immunofluorescent staining of neuromuscular junction of reinnervation of denervated gastrocnemius muscle with neurotization.

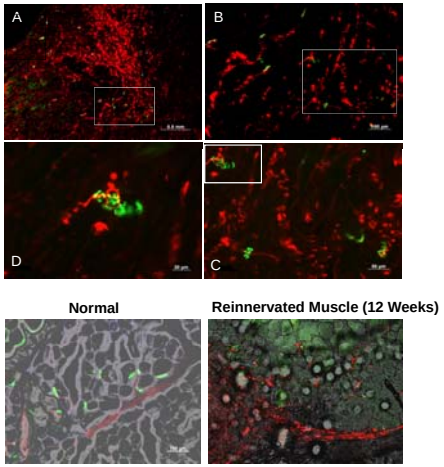

Figure 7. Immunofluorescent staining of neuromuscular junction of reinnervation of denervated gastrocnemius muscle at 12 weeks after neutization.

Conclusions

These studies indicate that, while nerve transplantation allows regeneration of the neuromuscular junction, the function of the denervated muscle remains in the subnormal range even at 12 weeks. These results suggest that nerve transplantation should be combined with other supportive treatment to allow for a more complete recovery of muscle function.

Acknowledgment

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