Regenerative Peripheral Nerve Interface (RPNI) and vascularized Denervated Muscle Targets (VDMT): a preclinical rabbit model as a translational feasibility and methodological platform

J. González Prieto; M. Arenillas Baquero; E. Sanz Barbero; A. Gutiérrez Pecharromán; J.D. Muñoz Frías; E. Alonso Rivas; M.C. Morillo Balsera; L. Cristóbal Velasco; R. Giannetti; A.A. Maldonado

Abstract-

Background

Regenerative Peripheral Nerve Interfaces (RPNIs) and Vascularized Denervated Muscle Targets (VDMTs) are emerging strategies for nerve regeneration and myoelectric prosthesis control. Most preclinical studies have been conducted in rodents, limiting the evaluation of implantable electromyographic devices due to anatomical and scale-related constraints. This study aimed to develop and evaluate the first RPNI and VDMT models in rabbits as a translational platform for implantable neuromuscular interfaces.

Methods

A total of 8 rabbits (4 per group) were randomly assigned to RPNI (n = 4) and VDMT (n = 4) groups and evaluated at an 8-week follow-up. RPNIs were created using biceps femoris muscle grafts attached to the peroneal nerve. VDMTs were constructed using denervated, vascularized gastrocnemius muscle flaps sutured to a peroneal motor branch. The contralateral leg served as a denervated control. Electrophysiological and histological analyses were performed 8 weeks postoperatively. Between-group comparisons were conducted using exact Mann–Whitney U and Fisher’s exact tests.

Results

VDMTs showed a trend toward better macroscopic vascularization and integration under the present experimental conditions. Electromyographic activity was detected in 3 of 4 VDMTs, whereas no signal was observed in RPNIs. Histological analysis demonstrated more favorable muscle tissue preservation in VDMTs, with no detectable necrosis (0% necrotic area in all specimens), while RPNIs exhibited substantial necrosis (20%–95% of the analyzed muscle area), which was significantly greater than in VDMTs (p = 0.0286). Neuroma formation occurred in all RPNIs and in 2 of 4 VDMTs.

Conclusions

This study presents a feasible rabbit model for the preclinical evaluation of RPNI and VDMT constructs. Under the present experimental conditions, VDMTs were associated with more favorable tissue preservation and more frequent signal detection under the present experimental conditions. These findings support the feasibility and translational potential of the rabbit as a methodological platform for future neuromuscular interface research. Further studies with optimized surgical protocols and larger cohorts are required to confirm these findings.

Index Terms- regenerative nerve interfaces; prosthetic control; rabbit model; interfaces nerviosas regenerativas; control protésico; modelo de conejo

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