DELAYED NERVE REPAIR NEGATIVELY AFFECTS PERIPHERAL NERVE REGENERATION AND FUNCTIONAL RECOVERY

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Introduction: nerve fibre regeneration and complete functional recovery after peripheral nerve injury do not always occur and can be influenced by many factors, including time interval that elapses before performing surgical repair. The aim of this study was to investigate the nerve regeneration after delayed repair and the degenerative processes of the denervated distal nerve stump.

Materials and methods: a rat surgical model of delayed nerve repair, consisting of a cross-suture between the chronically degenerated median nerve distal stump (3 and 6 months) and the freshly axotomized ulnar proximal stump, was used. Functional, morphometrical and biomolecular analyses were performed on regenerated distal nerve stumps 6 months after nerve repair.

Results: biomolecular analysis shows that, after chronic degeneration, Neuregulin1 (NRG1), a factor involved in Schwann cells survival and activity, is highly down-regulated, as well as some Schwann cell markers, thus suggesting that these cells undergo atrophy, as confirmed by ultrastructural analysis. After delayed nerve repair, functional recovery is compromised. Morphometrical analysis shows a significant reduction of the number and the size of regenerated myelinated fibres in the delayed repair groups. Finally, biomolecular analysis performed on the 6-months delayed group shows that soluble NRG1 is still strongly down-regulated after 6 months of regeneration.

Conclusions: despite a long delay, fibres are still able to regenerate, even if they are fewer and smaller. The poor outcome after delayed nerve repair might be explained by Schwann

cell impairment and their ineffective support for nerve regeneration. Moreover, the analysis of the NRG1/ErbB system shows a significant decrease of soluble NRG1 in degenerating nerves and in nerves after delayed repair, suggesting that NRG1 plays an important role in Schwann cell activity after denervation. These results suggest that providing a source of soluble NRG1 might be a good strategy to improve the outcome after delayed nerve repair.