ESWT and Nerve Regeneration

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What can we do?
Microsurgery: Autologous Nerve Transplant

- 30-40 cm transplant
- Nerve channels with activated Schwann cells
- Very slow regeneration

Since 1964

Prof. Hanno Millesi (1927-2017)

Fig. Interfascicular nerve grafting

Fig: Nerve transplant (Nervus suralis)
Understand the Mechanisms - The Repair Schwann cell

Suppression of myelin differentiation (de-differentiation):
- Downregulation of myelin genes
- Upregulation of markers of immature Schwann cells

Activation of repair phenotypes (alternative differentiation):
- Activation of trophic factors and surface proteins providing support for injured neurons and substrate for growth cones
- Formation of regeneration tracks (Bungner bands) for axon guidance
- Activation of cytokines and autophagy for myelin breakdown directly, and by macrophages

Repair Schwann cell: Regeneration

Adapted from Jessen and Mirsky 2016
Schwann cells: Two Activation States

Signaling Myelination

Schwann cells

MAG
P0

Myelinating

S100b

http://www.mc.vanderbilt.edu/
http://www.thomasjwestmusic.com/graphics/neuron.JPG

Mummenthaler, Stöhr, Müller-Vahl, 2007
Activated Schwann cells = Repair Schwann cells

How can we activate Schwann cells?
Improved rate of peripheral nerve regeneration induced by extracorporeal shock wave treatment in the rat

Thomas Hausner a,d,*, 1, Krisztián Pajer b,1, Gabriel Halat a,2, Rudolf Hopf a, Robert Schmidhammer a,c, Heinz Redl a, Antal Nógrádi a,b
Faster Axonal Regeneration after ESWT

Effect of ESWT on Schwann cells?

Hausner et al, 2012

http://www.szote.u-szeged.hu
Used Devices

Electro-hydraulic devices

Dermagold /Orthogold 100
Dermagold 180
Isolation of Schwann cells with ESWT

1. Dissect sciatic nerve
2. ESWT
3. Remove epineurium
4. Straining of nerve bundles
5. Collagenase digestion
6. Plate cells

3-10 mg

Without ESWT: Schwann cells get

ESWT: Expression of Activation Switch c-

- Reduced Senescence
- Prolonged activated state

Enhanced ATP release after ESWT in vitro

Adipose derived stem cells

Schwann cells

Schuh et al. 2016

Weihs et al. 2014

Chan et al. 2014
Take Home

• Schwann cells can be activated by ESWT
  – c-jun
  – p75
  – Proliferation
  – Reduced senescence

• ESWT accelerates nerve regeneration in an animal model reflecting the clinical reality
Clinical Study: ESWT after PNI

- 2 Hospitals (Meidling and Lorenz Böhler)
- Primary reconstruction of one or more digitalis nerves
- ESWT treatment within 48h
- Prospective, randomized, placebo controlled
- n=20
- 12 month follow up
Thank You!

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