Shock wave therapy enhances neuronal sprouting and improves neuronal survival

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Background:
Shock wave therapy (SWT) has been shown to induce tissue regeneration and improve function in spinal cord ischemia via TLR3. Thereby, induction of angiogenesis and alteration of microglial response could be observed. However, it remains unknown whether SWT exerts a regenerative effect on neurons, too. We aimed to analyze whether (1) SWT improves neuronal survival and enhances neurite growth and (2) TLR3 signaling is involved.

Methods:
Dorsal Root Ganglia (DRG) were isolated from Wild Type (WT) and TLR3 $^{-/-}$ mice and subsequently treated with SWT (0.01mJ/mm^2, 250 Impulses, 3Hz) or TLR3 agonist Poly(I:C). Control groups remained untreated. DRGs were analyzed via neuronal sprouting assay and survival was evaluated by TUNEL assay. Transmission electron microscopy (TEM) was used to evaluate the morphology of neurons and to assess vesicle release.

Results:
SWT lead to enhanced neurite growth and an increase of branch points (CTR 1433 ± 76.61 vs. SWT 2061 ± 151.5, $p<0.0001$). Treated neurons showed improved survival rates. SWT effects were missing in neurons isolated from TLR3$^{-/-}$ animals. Poly(I:C) treatment mimicked SWT effects. TEM analysis revealed release of microvesicles in treated neurons.

Conclusion:
SWT enhances neurite growth and improves neuronal survival via activation of TLR3. It could therefore develop as a potent therapeutic intervention for neuronal regeneration.