A pulsing electric field (PEF) increases human chondrocyte proliferation through a transduction pathway involving nitric oxide signaling

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Abstract

A potential treatment modality for joint pain due to cartilage degradation is electromagnetic fields (EMF) that can be delivered, noninvasively, to chondrocytes buried within cartilage. A pulsed EMF in clinical use for recalcitrant bone fracture healing has been modified to be delivered as a pulsed electric field (PEF) through capacitive coupling. It was the objective of this study to determine whether the PEF signal could have a direct effect on chondrocytes in vitro. This study shows that a 30-min PEF treatment can increase DNA content of chondrocyte monolayer by approximately 150% at 72 h poststimulus. Studies intended to explore the biological mechanism showed this PEF signal increased nitric oxide measured in culture medium and cGMP measured in cell extract within the 30-min exposure period. Increasing calcium in the culture media or adding the calcium ionophore A23187, without PEF treatment, also significantly increased short-term nitric oxide production. The inhibitor W7, which blocks calcium/calmodulin, prevented the PEF-stimulated increase in both nitric oxide and cGMP. The inhibitor L-NAME, which blocks nitric oxide synthase, prevented the PEF-stimulated increase in nitric oxide, cGMP, and DNA content. An inhibitor of guanylate cyclase (LY83583) blocked the PEF-stimulated increase in cGMP and DNA content. A nitric oxide donor, when present for only 30 min, increased DNA content 72 h later. Taken together, these results suggest the transduction pathway for PEF-stimulated chondrocyte proliferation involves nitric oxide and the production of nitric oxide may be the result of a cascade that involves calcium, calmodulin, and cGMP production.