Casper, D, et al. 2008. Pulsed Electromagnetic Fields Modulate cyclic GMP via a Nitric Oxide-Dependent manner in a Dopaminergic Neuronal Cell Line. Society for Neuroscience.

Abstract

There is currently no neuroprotective treatment for Parkinson's disease, where dopaminergic neurons in the substantia nigra degenerate. Experimental evidence provides several mechanisms by which neuronal survival might be increased that include; neurotrophic factor induction, calcium ion/protein interactions, and signal cascades initiated or regulated by nitric oxide (NO). Because these mechanisms of neuro-protection overlap with known actions of pulsed electromagnetic fields (PEMF), we are currently testing the potential of PEMF signals to influence neuroprotective pathways. Using a cell line of rodent dopaminergic neurons, we tested the effects of specific PEMF signals that were configured to enhance Ca2+ binding to calmodulin (Ca/CaM). We predicted this would activate Ca/CaM-dependent nitric oxide synthase (NOS), which in turn would modulate NO-sensitive guanylate cyclase (GC) to increase levels of cyclic GMP (cGMP). Experiments were performed using the dopaminergic MN9D cell line. Medium containing DMEM and 10% serum was changed to DMEM alone prior to PEMF treatment. Inhibitors of Ca/CaM (W-7), NOS (L-NAME), GC (ODQ), and PDE1 (8MM-IBMX) and vehicles were added when the medium was changed. PEMF signals consisting of 5 msec bursts of 27.12 MHz sinusoidal waves repeating at 5 bursts/sec, at 0.05 Gauss peak amplitude,configured a priori to modulate calcium binding to calmodulin were administered over 30 minutes. Control cultures were subjected to "null" signals under identical conditions. Conditioned media and cell lysates were collected at various times after PEMF treatment. NO was quantified indirectly by measuring NO2 with the Griess assay. Cyclic GMP was quantified by ELISA. NO2 concentrations in conditioned media increased from 0 to 1 micromolar over 5 hours. Cultures exposed to PEMF exhibited an accelerated increase in NO2 concentrations within the first 2 hours after treatment. Cyclic GMP synthesis increased up to 3-fold after PEMF treatment over the course of 5 hours. This effect was blocked by L-NAME, indicating that PEMF-induced cGMP production was dependent on NO synthesis. The PDE1 inhibitor 8MM-IBMX increased cGMP levels in both control and PEMF-treated cultures. Taken together, resultssuggest that PEMF signals can exert biological effects within neurons via Ca/CaM-dependent enzyme activation. Because alterations in both NO and cGMP levels can influence neuronal survival, future experiments will address more downstream events in the PEMF signal transduction cascade.