Neuroscience 278 (2014) 313–326

NEUROPROTECTIVE EFFECT OF WEAK STATIC MAGNETIC FIELDS IN PRIMARY NEURONAL CULTURES

M. BEN YAKIR-BLUMKIN,[a] Y. LOBODA,[a] L. SCHÄCHTER[b] AND J. P. M. FINBERG[a]*

[a] *Department of Molecular Pharmacology, Rappaport Faculty of Medicine, Technion – Israel Institute of Technology, 31096 Haifa, Israel*

[b] *Faculty of Electrical Engineering, Technion – Israel Institute of Technology, 32000 Haifa, Israel*

Abstract—Low intensity static magnetic fields (SMFs) interact with various biological tissues including the CNS, thereby affecting key biological processes such as gene expression, cell proliferation and differentiation, as well as apoptosis. Previous studies describing the effect of SMFs on apoptotic cell death in several non-neuronal cell lines, emphasize the importance of such a potential modulation in the case of neurodegenerative disorders, where apoptosis constitutes a major route via which neurons degenerate and die. In this study, we examine the effect of SMFs on neuronal survival in primary cortical and hippocampal neurons that constitute a suitable experimental system for modeling the neurodegenerative state *in vitro*. We show that weak SMF exposure interferes with the apoptotic programing in rat primary cortical and hippocampal neurons, thereby providing protection against etoposide-induced apoptosis in a dose- and time-dependent manner. Primary cortical neurons exposed to SMF (50 G) for 7 days exhibited a 57.1 ± 6.3% decrease in the percentage of cells undergoing apoptosis induced by etoposide (12 μM), accompanied by a marked decrease in the expression of the pro-apoptotic markers: cleaved poly ADP ribose polymerase-1, cleaved caspase-3, active caspase-9 and the phospho-histone H2A variant (Ser139) by 41.0 ± 5.0%, 81.2 ± 5.0%, 72.9 ± 6.4%, 42.75 ± 2.9%, respectively, and by a 57.2 ± 1.0% decrease in the extent of mitochondrial membrane potential collapse. Using the L-type voltage-gated Ca^{2+} channel inhibitor nifedipine, which is selective to Ca^{2+} influx through $Ca_v1.2$, we found that the anti-apoptotic effect of SMFs was mediated by Ca^{2+} influx through these channels. Our findings demonstrating altered Ca^{2+}-influx in response to thapsigargin stimulation in SMF-exposed cortical neurons, along with enhanced inhibition of KCl-induced Ca^{2+}-influx through $Ca_v1.2$ channels and enhanced expression of $Ca_v1.2$ and $Ca_v1.3$ channels, allude to the involvement of voltage- and store-operated Ca^{2+} channels in various aspects of the protective effect exerted by SMFs. These findings show the potential susceptibility of the CNS to weak SMF exposure and have implications for the design of novel strategies for the treatment and/or prevention of neurodegenerative diseases.

Key words: apoptosis, calcium influx, etoposide, neuroprotection, primary neuronal culture, static magnetic fields.

INTRODUCTION

Weak static magnetic fields (SMFs; 0.1–400 mT)[1] have raised a growing interest in recent years due to a wide variety of biological effects reported in both preclinical experiments (Ohkubo and Xu, 1997; Okano et al., 1999; Miyakoshi, 2005; Saunders, 2005), and clinical studies in