

LETTER TO THE EDITOR

**Electromagnetic field activation of voltage-gated calcium channels:
role in therapeutic effects**

Martin L. Pall

School of Molecular Biosciences, Washington State University, Pullman, WA, USA

Prof. Pilla (2013) presents a well-documented and highly integrated model of non-thermal therapeutic effects of pulsed/modulated electromagnetic fields (EMFs). The model involves increased intracellular Ca^{2+} , stimulation of calmodulin-dependent signaling both via Ca^{2+} elevation and via direct EMF effects on calmodulin, Ca^{2+} /calmodulin stimulation of cNOS activity/nitric oxide (NO) elevation/stimulation of the cGMP signaling pathway. Increased intracellular Ca^{2+} produced by EMF exposure was already well documented over 20 years ago (Walleczek, 1992) and the only concern of this letter is the origin of such increased intracellular Ca^{2+} in Prof. Pilla's model.

It has been shown in two dozen studies of EMF effects mostly at the cellular level, that effects of EMF exposure can be blocked by calcium channel blockers, demonstrating that activation of voltage-gated calcium channels (VGCCs) appears to be essential for many and perhaps all EMF responses (Pall, 2013). It may be argued, therefore, that the increased intracellular Ca^{2+} in Prof. Pilla's model is likely to come from such VGCC activation. While it was proposed that EMF-mediated VGCC activation may be due to partial depolarization of the plasma membrane (Pall, 2013), it is equally plausible that the direct influence of EMFs on the charged residues that regulate VGCC channel opening (Catterall, 2000), may be an alternative explanation.

There is one other possible implication of this EMF-VGCC study. While therapeutic effects were proposed to

occur via a very similar pathway of action to that proposed by Prof. Pilla (2013), it was also proposed that pathophysiological effects of EMFs may be produced via reaction of NO with superoxide to form peroxynitrite, a potent oxidant (Pall, 2013). If this proposal is correct, it may be useful in therapy to use agents that lower superoxide, such as by Nrf2 induction, and perhaps other agents that lower peroxynitrite, to avoid pathophysiological responses to EMF exposure during such therapy.

Declaration of interest

The author reports no conflicts of interest and is solely responsible for the writing and content of the article.

References

- Catterall, W. A. (2000). Structure and regulation of voltage-gated Ca^{2+} channels. *Annu. Rev. Cell Dev. Biol.* 16:521–555.
- Pall, M. L. (2013). Electromagnetic fields act via activation of voltage-gated calcium channels to produce beneficial or adverse effects. *J. Cell Mol. Med.* 17:958–965.
- Pilla, A. A. (2013). Nonthermal electromagnetic fields: From first messenger to therapeutic applications. *Electromagn. Biol. Med.* 32: 123–136.
- Walleczek, J. (1992). Electromagnetic field effects on cells of the immune system: The role of calcium signaling. *FASEB J.* 6: 3177–3185.