Neuromodulation by Exposure to a Pulsed Low Frequency Magnetic Field

A. W. Thomas[1], J. Robertson[2], F. S. Prato[3]

Imaging Program, Lawson Health Research Institute, St. Joseph's Health Care, London, Ontario, Canada N6A 4V2
[1]athomas@lawsonimaging.ca
[2]jroberts@lawsonimaging.ca
[3]and Diagnostic Imaging, prato@lawsonimaging.ca

Abstract

Exposure to a relatively weak (100 to 1000 microTesla) low frequency (< 1000 Hz) specific pulsed magnetic field (CNP) has produced analgesia (antinociception) in snails, mice, and humans, and altered normal resting EEG in human subjects. We have also shown changes in human brain activation using fMR(BOLD) imaging due to a specific pulsed CNP exposure applied through the MR gradient coils. The alteration in brain activation corresponds to regions of interest associated with the affective processing of pain signaling.

Introduction

Neuromodulation, the alteration of neuronal activity through electrical or magnetic stimulation, is proving to become one of the most effective means of selectively altering brain and spinal cord activation for some conditions. While electrical stimulation such as deep brain stimulation (DBS) is still an extremely invasive technique, new and novel forms of magnetic stimulation leading to neuromodulation are non-invasive and hold the promise of being versatile enough for individualized therapy in the near future. CNPs have been applied to snails, mice, and humans [1-6] in previous studies and most recently a method of exposing humans to CNPs during functional magnetic resonance imaging utilizing blood oxygen level dependence (fMRI(BOLD)) has been developed with specialized MRI gradient system programming.

Methods

The CNP is an arbitrary waveform (see Figure 1, USPTO # 6,234,953 Fralex Therapeutics Inc. Toronto Ontario Canada) presented as a time-varying magnetic field normally produced through Helmholtz coils [7-8] or head coils [9]. Here we utilized the gradient coils within a Siemens Avanto 1.5 Tesla MRI system to apply a 200 microTesla (peak) magnetic field midbrain, with a 10 cm gradient to 0 microTesla CNP. In this latest study subjects were tested at their thermal pain threshold [9] on the hypothenar eminence of the hand in an fMRI(BOLD) paradigm and then exposed to either the CNP or a sham exposure while in the MRI system, and then again tested at the thermal pain threshold during the fMRI(BOLD) paradigm. The CNP or SHAM condition (no CNP) was applied for 15 min between the Pre-exposure fMRI(BOLD) thermal pain imaging session and fMRI(BOLD) thermal pain Post-exposure imaging session Several regions of interest (ROIs) were selected for analysis relating to the affective processing of pain, including executive function (posterior cingulate (see Fig 2)) and pain processing (anterior cingulate (not shown).

Results

Significant alteration of brain activation in the ROIs associated with pain processing and executive function were evidenced after receiving 15 min of exposure to the CNP as compared to the SHAM (Post-exposure fMRI(BOLD) signal minus Pre-exposure fMRI(BOLD) signal at $P < 0.05$) (see Fig 2 for visual comparison). Additional ROIs were likewise examined and provide significant evidence of alteration of fMRI(BOLD) signal (not shown here, see URSI GA 2008 symposium paper by Robertson et al).

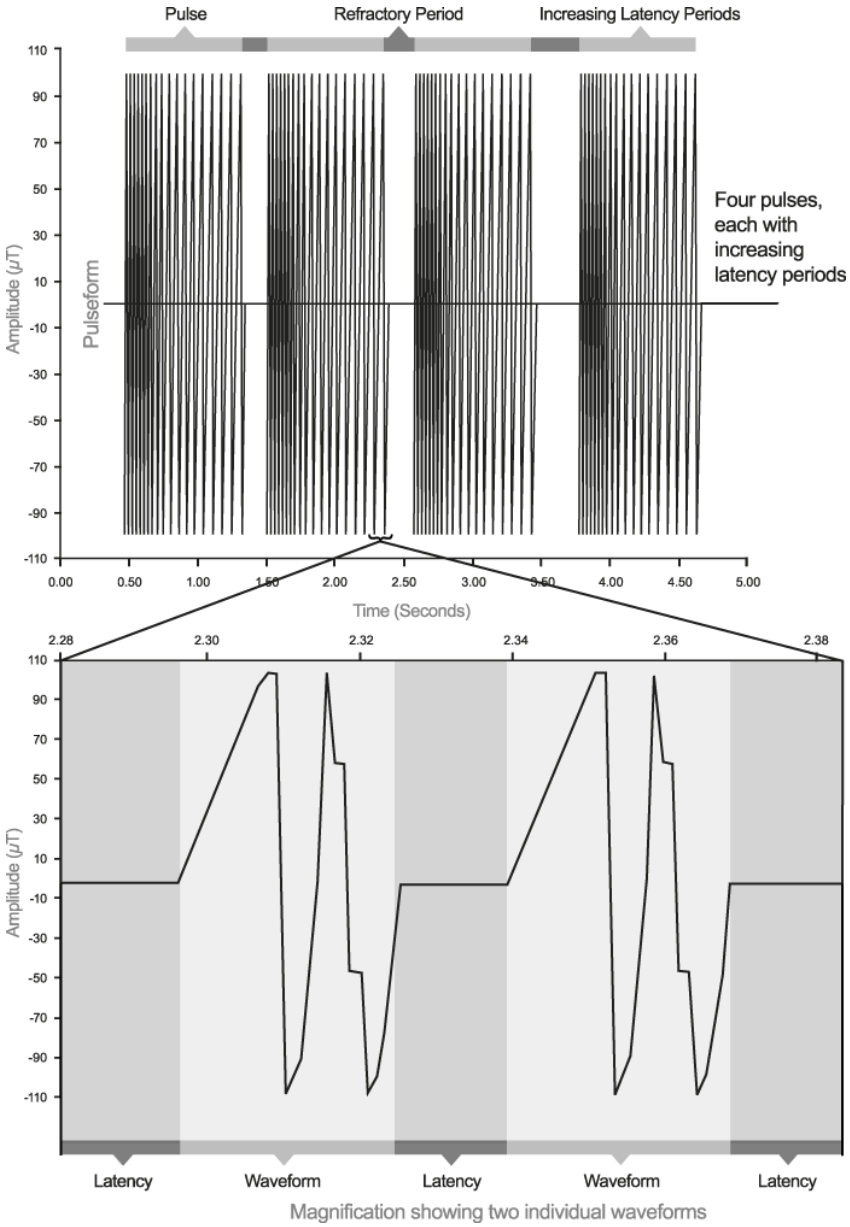

Figure 1: CNP recording (mid-brain, in non-magnetic head phantom, 100 microTesla (peak)). Each individual waveform is separated by a latency period and combined in sets to produce pulse trains containing waveforms, latency periods, and refractory periods (see USPTO #6,234,953). Reprinted with the permission of Fralex Therapeutics Inc (Toronto, Ontario, Canada).

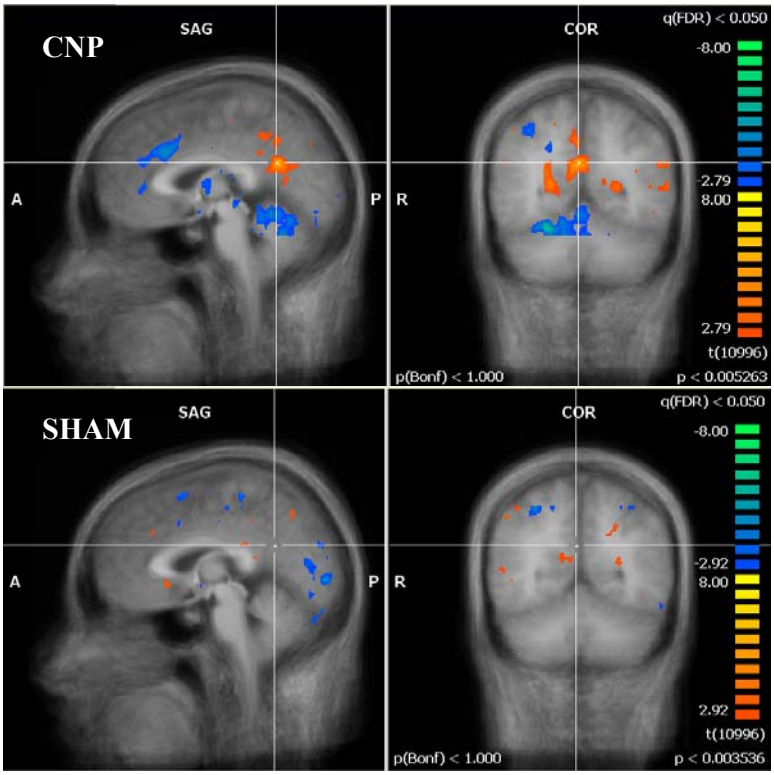

Figure 2: Posterior cingulate (N=31, CNP=14 (upper set), Sham=17 (lower set)) imaged (fMRI(BOLD)) with pre-exposure brain activation subtracted from post-exposure brain activation. All activation shown is significant ($P < 0.05$) and has been corrected for multiple tests using the FDR method (Brain Voyager). Anatomical images have been averaged for all subjects (thus the fuzzy appearance) to more accurately represent true anatomical placement within the studied group. Increases in fMRI(BOLD) signal (activation) is evidenced from yellow-red coloration, while decreases in signal are evidenced by blue-green coloration.

Discussion

Previous human studies have utilized 2m Helmholtz coil designs and head-worn coils which produce equivalent therapeutic success [9-11]. Here, the CNP was delivered within a 1.5 Tesla MRI environment, which means that the effects of the 200 microTesla CNP was evident even though there was the 1.5 Tesla static MF, the gradient MF, and the imaging RF MF produced during the protocol as well as the CNP. This leads to an intriguing hypothesis that the CNP effects are related the 'information' provided by the waveform, and not the MF exposure itself as a tissue-transduced non-specific MF signal, or a generalized response to MF. Further data analysis and research will explore this hypothesis.

Acknowledgments

We would like to specially thank Dr. Jean Theberge for the Siemens Avanto gradient system programming, Dr. Derek Mitchell for image processing advice, and Fralex Therapeutics for permission to use their CNP waveform and Figure 1. Funding was provided by the Natural Sciences and Engineering Research Council of Canada (NSERC), the Canadian Institutes of Health Research (CIHR), Ontario Research and Development Challenge Fund (ORF), and Fralex Therapeutics Inc (FTI).

Statement of Conflict of Interest: Drs Alex Thomas and Frank Prato are co-founders of and shareholders in FTI. Dr. Thomas is V-P Research for FTI. Mr. John Robertson receives a student stipend and research support from FTI. FTI is a publicly traded company on the Toronto Stock Exchange [TSX:FXI]. See (www.fralex.com) for details.

References

1. NM Shupak, FS Prato, AW Thomas. Therapeutic uses of pulsed magnetic field exposure: a review. *URSI: Radio Science Bulletin* **307**(Dec), 2003, pp. 9-32.
2. NM Shupak, FS Prato, AW Thomas. Therapeutic uses of pulsed magnetic field exposure (updated review). *WHO/ICNRP/ URSI Proceedings* (Sevilla, Spain, May 20-22, 2004) Session 5b:1-15, 2004.
3. NM Shupak, J Hensel, S Cross-Mellor, M Kavaliers, FS Prato, AW Thomas. Analgesic and behavioral effects of a 100 μT specific pulsed extremely low frequency magnetic field on control and morphine treated CF-1 mice. *Neurosci Lett* **354**(1), 2004, pp. 30-33.
4. JC McKay, FS Prato, AW Thomas. A Literature Review: The Effects of Magnetic Field Exposure on Blood Flow and Blood Vessels in the Microvasculature. *Bioelectromagnetics* **28**(2), 2007, pp 81-98.
5. CM Cook, AW Thomas, FS Prato. Human Electrophysiological and Cognitive Effects of Exposure to ELF Magnetic and ELF modulated RF and Microwave Fields: A Review of Recent Studies. *Bioelectromagnetics* **23**, 2002, pp. 144-157.
6. CM Cook, DM Saucier, AW Thomas, FS Prato. Exposure to ELF magnetic and ELF modulated radiofrequency fields: the time course of physiological and cognitive effects observed in recent studies (2001-2005). *Bioelectromagnetics* **27**(8), 2006, pp. 613-627.
7. AW Thomas, DJ Drost, FS Prato. Human subjects exposed to a specific (200 μ T) magnetic field: effects on normal standing balance. *Neurosci Lett* **297**(2), 2001, pp. 121-124.
8. NM Shupak, J Hensel, FS Prato, AW Thomas. Effects of exposure to a specific pulsed magnetic field on thermal sensory thresholds in humans. *Neursci Lett* **363**(2), 2004, pp. 157-162.
9. NM Shupak, JC McKay, WR Nielson, GB Rollman, FS Prato, AW Thomas. Effects to a specific pulsed low-frequency magnetic field: a double-blinded placebo controlled study of effects on pain ratings in rheumatoid arthritis and fibromyalgia patients. *Pain Research and Management* **11**(2), 2006, pp. 85-90.
10. AW Thomas, KP White, DJ Drost, CM Cook, FS Prato. A comparison of rheumatoid arthritis (ra) and fibromyalgia (fm) patients and healthy controls exposed to a pulsed (200μT) magnetic field: effects on normal standing balance. *Neurosci Lett* **309**(1), 2001, pp. 17-20.
11. AW Thomas, FS Prato, K Graham, P Morley Forster, D Moulin, S Chari. A pilot trial in chronic musculoskeletal pain: double-blinded placebo-controlled treatment with a specific low frequency pulsed magnetic field. *Pain Research and Management* **12**(4), 2007, pp. 249-258.