Simultaneous EEG/EMG/fMRI: a powerful hybrid-imaging window on brain activation patterns during and following time-varying magnetic stimuli

Alexandre Legros[1], Jill Cates[1], John Robertson[1], Julien Modolo[1], Nicole Juen[1], Jodi Miller[1], Frank Prato[1], Alex Thomas[1]

[1] Bioelectromagnetics Group, Imaging Program, Lawson Health Research Institute, St. Joseph's Health Care, 268 Grosvenor Street, N6A 4V2, London, Ontario, Canada. alegros@lawsomimaging.ca

Abstract

Bioelectromagnetics is a rapidly expanding research domain investing the interaction between electromagnetic stimuli and biological systems. Hybrid functional imaging is a growing domain with promising developments, opening new multidimensional windows on brain processing. Our group started to use functional Magnetic Resonance Imaging (fMRI) in counter-balanced blinded studies to investigate the effects of magnetic field exposure on brain activation in specific tasks. Results showed modulations of task-induced brain activation associated with exposure, suggesting increased haptic sensitivity. We are now proceeding to the next step by integrating electroencephalography, electromyography and fMRI to study exposure levels generating magnetophosphenes in healthy volunteers.

1. Introduction

Hybrid functional imaging provides a novel approach in neuroimaging that opens new windows into the study of the complex connectivity within the brain. The simultaneous measurement of electrical and metabolic activity of living tissue at different temporal and spatial scales is a key factor in disentangling the interactive mechanisms of electromagnetic fields on biological systems. Individual imaging techniques (i.e., electroencephalography, EEG; and functional magnetic resonance imaging, fMRI) have limited potential due to the trade-off between spatial and temporal resolution. Thus, a combination of these imaging techniques can maximize the detection of the effects of specific stimuli with high temporal and spatial resolutions. In our Bioelectromagnetics Group, simultaneous EEG/fMRI techniques are used as a hybrid tool to investigate brain activation following brain stimulation from MF exposure, and the integration of EMG (electromyography) is currently being processed.

2. Imaging Techniques

2.1 EEG

EEG is a non-invasive approach to neuroimaging that measures the summation of the excitatory and inhibitory post synaptic potentials from the cortical layer [1]. Surface EEG involves the placement of electrodes on the scalp to estimate the synaptic action averaged over millions of neurons. This imaging technique offers high temporal resolution while providing one of the most direct non-invasive measures of electrical activity in the brain. EEG time series are classically analysed in the frequency domain and characterized in terms of power content within delaminated frequency bands. Source localization methods are also available for determining the cortical origin of the recorded electrical brain activity. However, these methods have limited spatial resolution, which is a major shortfall of the EEG technique [2]. Source localization is achieved by solving the inverse problem and specialized software packages such as CURRY (Compumedics-Neuroscan, Charlotte, NC) are developed for this purpose. They can provide a spatial resolution on the order of cm^2 for surface recording and cm^3 for sources, thus providing a reasonably accurate estimate of the EEG source.

2.2 Functional MRI

Functional Magnetic Resonance Imaging (fMRI) is a valuable functional imaging technique that relies on hemodynamic activity to measure functional brain activity. Local brain activation causes an increase in metabolic demand, thus resulting in a compensatory increase in the oxygenated blood levels of that local region as compared to the resting state. Functional MRI measures activation in the brain by distinguishing between the magnetic properties

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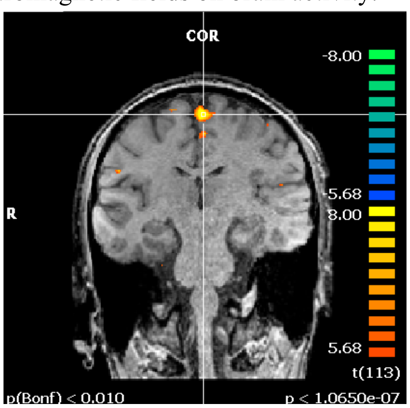
of oxygenized and deoxygenized blood. The magnetic moment of oxygenated blood is lower than deoxygenated blood, which leads to a slight signal difference that depends on the blood oxygenation. This type of MR imaging is described as a Blood Oxygenation Level Dependent (BOLD) signal [3]. The BOLD technique depends on small changes in signal magnitude, which requires fMRI studies to use multiple repetitions of a stimulus in order to detect the functional changes. Thus, fMRI is most suitable for imaging repeated acute stimuli over relatively short time periods (i.e., in seconds). Though fMRI offers high spatial resolution of brain activity, it severely compromises in temporal resolution due to the slow measurement of BOLD signal differences.

2.3 Hybrid functional imaging

Individual neuroimaging modalities such as EEG and fMRI present a trade-off between spatial and temporal resolution. EEG is a direct measure of electrical potentials of synaptic activity in the brain with high temporal resolution on the order of tens of milliseconds. However, it presents the inverse problem, which limits spatial discrimination of the area of the brain that produced a specific electrical recording. Functional MRI is able to precisely determine the location of brain activity, but it is an indirect and delayed hemodynamic model of brain activity with limited temporal resolution. Hybrid functional imaging is a cutting-edge approach that combines modalities such as EEG, fMRI, EMG (electromyography) and even EKG (electrocardiography), (see Figure 1 for an example of EEG/EMG/fMRI data). Combined EEG/fMRI systems can measure brain activity with a high level of temporal and spatial accuracy, thus allowing bioelectromagnetic researchers to thoroughly investigate the effects of electromagnetic fields on brain activity.

(A)


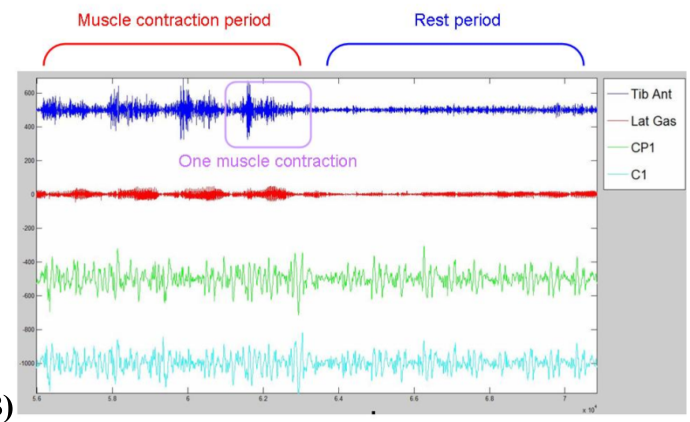
(B)


Figure 1: An example of a simultaneous EEG/EMG/fMRI system during a rest task with intervals of muscular contraction in a single test subject. (A) fMRI-BOLD activation within the motor cortex represented by the bright regions at the center of the crosshairs. (B) EMG and EEG recorded during one repetition of the muscle contraction and rest task.

3. Contributions of Imaging Techniques in Bioelectromagnetics Research (Current Studies from our Bioelectromagnetics Group at 60 Hz – Phase II)

In the initial Phase of our 60 Hz bioelectromagnetics program, the effects of extremely low frequency (ELF) magnetic field (MF) exposure on behaviour and neurophysiological function were investigated in human studies conducted with a 1.8 mT, real/sham protocol. Phase I focused on the physiological effects of MF and only introduced the use of fMRI in 60 Hz human studies through a pilot study with 9 subjects. Overall, the results from Phase I suggest that ELF MF does not modulate cardiovascular parameters, resting EEG activity, or voluntary rhythmic movement control [4]. However, our results indicate a subtle MF effect that increases physiological tremor amplitude in the frequency band known to be associated with central nervous system input. Furthermore, MF exposure was associated with a decrease in standing balance oscillations, as previously reported by our group [5]. This effect was reported only during the 'eyes closed' condition, which suggests that the exposure may act on proprioceptive or vestibular functions [6]. The pilot fMRI study of Phase I was a real/sham counter-balanced blinded study. In the sham condition, the subjects were treated with the same protocol as in the real exposure condition, but were never exposed to the MF. In order to conduct the pilot study, we programmed our MRI scanner (1.5 T Advanto at the time, Siemens, Germany) to become an active exposure device which generated the 60 Hz MF using its Z-gradient coil. The results showed that the level of brain activation induced by the finger-tapping task was higher post-exposure (n=4) as compared to post-sham (n=5) [7]. Phase II further investigated the results of the pilot project by examining the effect of a 3 mT MF at 60 Hz on human brain activation during a finger-tapping task, during a mental rotation task and at rest. The protocol of Phase II extended the exposure period from 30 minutes to 1 hour and increased the MF magnitude from 1.8 to 3 mT. The results showed a higher level of task-induced brain activation in the primary somatosensory motor cortex (S1 -Figure 2) and in the cerebellum during the MF exposure condition as compared to the sham condition. This finding suggests an improved haptic sensitivity, thus indicating an increased level of perception of the tactile sense. Moreover, this study suggests that MF exposure reduces the level of activation in regions associated with visual attention while completing a mental rotation task [8]. This finding could be indicative of a facilitation of visual attention processes with MF exposure.

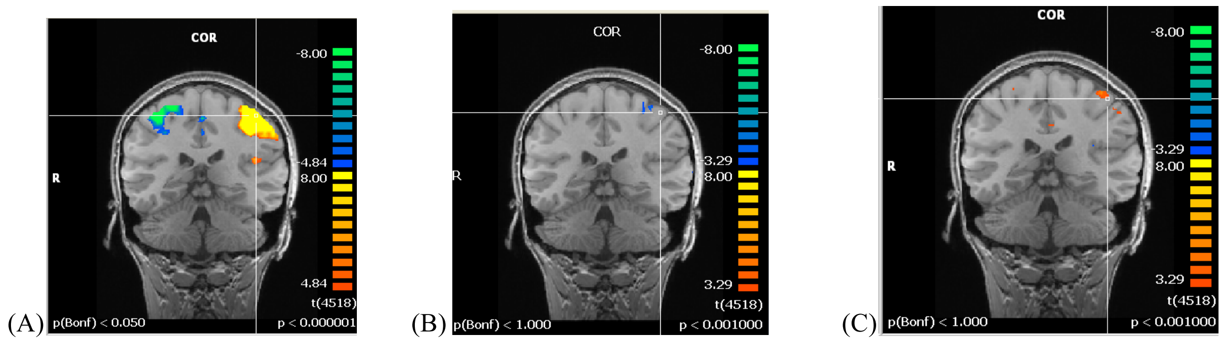


Figure 2: (A) Motor cortex activation measured by fMRI during an index finger-tapping task and averaged over 20 subjects. (B) Differential activation map (post-exposure *minus* pre-exposure images) from the sham exposed group (n=11). (C) Differential activation map (post-exposure *minus* pre-exposure images) from the real exposed group (n=9).

Based on the results of Phase I and II, the effects of MF at 60 Hz can be identified at the level of human cognition and functional brain activation. These effects are persistent after the exposure offset and appear to interfere with learning processes at 3 mT, which may indicate an effect on synaptic plasticity. The results also show that a simple motor task can be modulated during (tremor and standing balance, 1.8 mT) and after (tapping, both 1.8 and 3 mT) 60 Hz MF exposure. Furthermore, MF exposure appears to interact with perceptive pathways that include the proprioceptive and vestibular systems. However, the effects are subtle and the underlying mechanisms are not accessible if the imaging approach is adapted to detect the subtle proprioceptive and vestibular effects. The perception of magnetophosphenes is reported as a well-established and consistent interaction between ELF MF and the central nervous system in humans [9]. Magnetophosphenes are characterized as flickering lights that can be perceived with eyes closed in a dark environment when the retina is exposed to MF between 5-20 mT, depending on the frequency [10]. Phase III will examine the effects of a 60 Hz MF of up to 50 mT (local cortical and global head exposures) on the perception of magnetophosphenes. A section of the protocol will use EEG and fMRI (sequentially and simultaneously, EEG during exposure) and evoked related potentials (ERPs). EEG recordings and fMRI activity will be investigated at exposure levels inducing phosphenes in exposed volunteers.

4. Fusing EEG and fMRI as a Hybrid Functional Imaging Modality (Future Work of our Bioelectromagnetics Group at 60 Hz – Phase III)

Phase III will focus on the potential changes in resting brain activation patterns between short repeated exposure periods (vs. no exposure in Phase II). The MF exposure amplitude will be increased from up to 8 mT in which continuous and intermittent exposure patterns will be investigated. In the protocol for intermittent exposure, BOLD images will be interleaved between the exposure sequences (sham and real exposures alternatively presented to allow the acquisition of BOLD images). EEG will be recorded simultaneously with fMRI-BOLD using a NeuroScan MRI-compatible EEG system while the subjects have their eyes closed. We will compare: (1) human resting EEG with and without exposure (real and sham conditions, including EEG during 60 Hz exposure) using a sequence alternating 2-second epochs of 60 Hz exposure and 2-second epochs of sham exposure; and (2) brain functional activation as measured by fMRI at rest after either 10-second exposure periods or 10-second sham exposure periods (with at least 10 repetitions for each condition). The underlying assumption of this protocol is that the short-term effect of intermittent 60 Hz MF exposure is the detectable stimulus and overrides any carryover effect that may occur. The Z-gradient coil of the fMRI scanner is used to generate the 60 Hz MF and therefore, it is not possible to acquire fMRI images during MF exposure. To minimize the period between exposure and imaging acquisition, a specific stand-alone sequence that integrates fMRI imaging and 60 Hz MF exposure sequences will be programmed. The subject will report any visual sensation by pressing an MRI-compatible button press to follow up on the perception of magnetophosphenes. These magnetophosphenes can then be linked to the EEG and fMRI data, thereby offering the opportunity to provide a detailed quantitative description of the neurological patterns associated with magnetophosphenes. Furthermore, in combination with the previously described electrophysiological interaction study, EEG will be recorded during exposure. Note that we have now completed a few experiments dealing with time-varying MF exposure given within an MRI environment, and we have already started integrating EEG as an additional available measurement within this context [11].

5. Concluding Remarks

Previous studies have indicated the potential for electromagnetic fields to affect neurophysiological, motor and cognitive functions, but the effects are subtle and difficult to characterize. Hybrid functional imaging offers a solution to the limitations of bioelectromagnetics research: it can measure brain activity with both high temporal and spatial resolution. Our group is developing EEG/EMG/fMRI imaging protocols to study the effects of MF on brain processes. Our current challenge is to use this multimodal imaging technique to approach the neurological patterns associated with magnetophosphene perception during MF exposure, and to investigate synaptic transmission during MF exposures in the milliTesla range.

6. References

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