ISMRM Conference, Montreal

Session: Combined MRI, 12 May 2011, 10:30

MRI/EEG

Jean Gotman, PhD, Montreal Neurological Institute, McGill University

Introduction. Functional MRI (fMRI) studies are usually performed in the context of sensory stimuli or cognitive tasks. By contrasting the BOLD signal following the stimulation or task with a rest period, it is possible to assess the part of the brain involved specifically in these events. It is also possible to replace the stimulation or task by events that occur in a physiological measure, so that it is possible to find the source of cerebral activity related to this measure. One such measure is the EEG. Despite the magnetically very hostile environment of a high static field and rapidly changing field gradients, it is possible to record inside the scanner EEG signals with an amplitude of just tens of microvolts. The changing EEG signal can then be used to drive the fMRI analysis.

The main application of EEG-fMRI is in the study of epilepsy, where it is possible to find the BOLD concomitants to the epileptic discharges visible on EEG. This provides a non-invasive functional investigation of the whole brain at the time of an epileptic discharge, something that no other method can provide. EEG-fMRI is also used to study brain activity in relation to various spontaneous brain rhythms, such as alpha activity or sleep spindles, or with sensory or cognitive tasks, where the high spatial resolution of fMRI combines with high temporal resolution of the EEG.

EEG Recording. The equipment required to record the EEG in the MR scanner without affecting significantly image quality includes non-magnetic electrodes (typically silver-silver chloride) and electrode wires, an MR compatible amplifier system that is battery operated and transmits the EEG outside the scanner room with an optic fiber so that shielding is preserved. The recording computer and control consol are located outside the scanner room. Electrode wires around the patient head and until the amplifier must be immobilized since the smallest wire movement within the high field causes an important artifact in the EEG (induced current). It is also important to use padding around the electrodes for patient comfort. During EPI scanning, the high magnetic gradients induce an artifact that completely obscures the EEG. It is nevertheless possible to remove this artifact because it is an extremely repeatable event. Another important artifact in the EEG is caused by the ballistocardiogram (small movement of the electrodes as a result of the blood pressure wave. Once these artifacts are removed by signal processing techniques, it is possible to retrieve an EEG of reasonable quality, although not as clean as an EEG recorded in the usual conditions.

If it is considered possible that a patient may have seizures, then it is important to take precautions: monitor the patient's face with video and be ready to take rapidly the patient out of the scanner.

Analysis of the BOLD Signal. In the context of the application of EEG-fMRI to epilepsy, the epileptic events are marked in the EEG by an experienced electroencephalographer after the artifacts have been removed. The time of these events are then used in a classical event-related fMRI analysis: an impulse is placed at the time of each event, this impulse is convolved with a hemodynamic response function (HRF) and an analysis following a General Linear Model (GLM) is performed. A few points need attention:

- The fMRI study is often long (30 to 90 minutes) in order to increase the chance of recording epileptic events (these are unpredictable and can be infrequent). It is thus not infrequent that there is some head movement. Motion correction can be applied to the EPI images, but it is also important to enter the motion parameters (x, y, z) as confounds in the GLM analysis because motion cannot be totally corrected.
- Epileptic events do not always have a HRF that conforms to that most commonly seen in sensory or cognitive experiments. It has therefore been proposed that multiple HRFs be used in the analysis; for example a canonical HRF and its derivative, or a series of HRFs peaking at different times,e.g. 3, 5, 7 and 9 seconds.
- Most epileptic events are of very short duration (50 to 200 ms) and can be considered instantaneous for the purpose of fMRI analysis. If the event is longer (e.g. burst of spike and wave), the HRF should be convolved with a boxcar function having the duration of the event rather than with an impulse function.
- As for all fMRI studies, better results are obtained with a higher field strength (3T rather than 1.5T), although the higher strength results in a worse ballistocardiographic artifact.

Application to Epilepsy. Many studies in the last 10 years have demonstrated that the BOLD response to epileptic events in the EEG is maximum in the region likely to be generating the event. Studies have been performed in focal and in generalized epilepsies, in adults and children. While most studies report interictal epileptic events, a few studies report the analysis of epileptic seizures and these appear to be particularly informative. Seizures with significant movement cannot be analyzed but it is possible to analyze brief seizures, some of which have no or very minimal clinical accompaniment, such as sensory auras. A few noteworthy results from these studies:

- If the patient has no epileptic event during the study, no analysis can be performed. It is recommended to select only patients likely to have at least a few events during the scan.
- In focal epilepsy, BOLD responses can be helpful in the localization of an epileptic focus, particularly in patients with non-lesional focal epilepsy.
- BOLD responses are also seen at a distance from the focus, most likely representing the propagation of epileptic activity to remote brain regions.
- While most responses are activations, it also happens that deactivations take place, either at the focus or more often at a distance from it. The reason for this is not always clear.
- In generalized epileptic discharges, the suspension of the Default Mode Network has been observed, possibly underlying decreased consciousness during these events.

Application to Resting EEG. A few studies have addressed the relationships between normal fluctuations in the EEG and the BOLD signal. It has for instance been found that the alpha rhythm, prominent in occipital regions when the subject is at rest with the eyes closed, is accompanied by a clear increase in BOLD signal in the thalamus and a decreased BOLD signal in the occipital cortex, reflecting the "rest" or idling of the visual cortex when the eyes are closed. Studies have also demonstrated the relationship between fluctuations in theta and gamma activity and the Default Mode Network.

Note: EEG Electrodes and MRI. Independently of the combined study of EEG and fMRI, it is interesting to note that MRI-compatible EEG electrodes have been developed and are currently in use in several institutions. The advantage of these electrodes is that it is possible to obtain an MRI scan of excellent quality (typically an anatomical scan) without having to remove EEG electrodes, an important advantage in patients who are subject to long-term EEG monitoring, either in the context of epilepsy evaluation or in the intensive care unit.

Conclusion. Combining EEG and fMRI is not a simple procedure. The placement of the electrodes and of the patient in the scanner are delicate and time consuming. The removal of the artifact from the EEG, the EEG interpretation and the GLM analysis require expertise. The results can fortunately be rewarding, particularly in the evaluation of difficult epileptic patients.

Selected Bibliography - Reviews

Gotman J, Kobayashi E, Bagshaw AP, Bénar CG, Dubeau F. Combining EEG and fMRI: A Multimodal Tool for Epilepsy Research. *Journal of Magnetic Resonance Imaging* 23:906-920, 2006.

Laufs H, Duncan J. Electroencephalography/functional MRI in human epilepsy: what it currently can and cannot do. *Current Opinion in Neurology* 2007, 20:417–423.

Simultaneous EEG-fMRI in human epilepsy. Cunningham CJ, Zaamout Mel-F, Goodyear B, Federico P. Can J Neurol Sci. 2008 Sep;35(4):420-35

Simultaneous EEG and fMRI: Recording, Analysis and Application, edited by Markus Ullsperger, Stefan Debener, 336 pp., Oxford University Press, 2010.

Selected Bibliography – Recent Papers

Noninvasive dynamic imaging of seizures in epileptic patients. Tyvaert L, LeVan P, Dubeau F, Gotman J. Hum Brain Mapp. 2009 Dec;30(12):3993-4011

Simultaneous EEG-fMRI in drug-naive children with newly diagnosed absence epilepsy. Ekstrom A, Suthana N, Millett D, Fried I, Bookheimer S. J Neurophysiol. 2009 May;101(5):2668-78.

Simultaneous EEG, fMRI, and behavior in typical childhood absence seizures. Berman R, Negishi M, Vestal M, Spann M, Chung MH, Bai X, Purcaro M, Motelow JE, Danielson N, Dix-Cooper L, Enev M, Novotny EJ, Constable RT, Blumenfeld H. Epilepsia. 2010 Oct;51(10):2011-22.

Reproducibility of interictal EEG-fMRI results in patients with epilepsy. Gholipour T, Moeller F, Pittau F, Dubeau F, Gotman J. Epilepsia. 2010 Nov 3. doi: 10.1111/j.1528-1167.2010.02768.x.

EEG correlated functional MRI and postoperative outcome in focal epilepsy. Thornton R, Laufs H, Rodionov R, et al.J Neurol Neurosurg Psychiatry. 2010 Aug;81(8):922-7.

EEG-fMRI: adding to standard evaluations of patients with nonlesional frontal lobe epilepsy. Moeller F, Tyvaert L, Nguyen DK, LeVan P, Bouthillier A, Kobayashi E, Tampieri D, Dubeau F, Gotman J. Neurology. 2009 Dec 8;73(23):2023-30.

Correlation between BOLD fMRI and theta-band local field potentials in the human hippocampal area. Ekstrom A, Suthana N, Millett D, Fried I, Bookheimer S. J Neurophysiol. 2009 May;101(5):2668-78. Epub 2009 Feb 25.