DTI Fiber Tracts Connect Epileptic Networks Imaged with MEG Coherence Analysis

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Abstract

The objective of this study was to determine if Diffusion Tensor Imaging (DTI) tractography can image epileptic networks connecting areas of high coherence identified with MEG imaging. Synchronization of neuronal activity, characteristic of epileptic activity, can be quantified by coherence between cortical sites. DTI quantifies water molecule diffusion and also the degree and direction of anisotropy. Cerebral tissue has highly heterogeneous diffusion anisotropy therefore tractography can identify pathways of major nerve fiber tracts. Combining MEG and DTI can lead to better understanding of epileptic networks and their connectivity. For ten epilepsy patients spontaneous MEG data (sampled at 508 Hz, from 0.1 to100 Hz, forward and backward filtered using a 3-50 Hz bandpass) were acquired. The MR-FOCUSS-ICA technique was used to image the MEG data. Coherence spectra were calculated for frequencies below 50 Hz. DTI scans were acquired (25 directions, 2.6 mm slices, b0=1000 s/mm^2) and processed using MedINRIA (Asclepios Research Project - INRIA Sophia Antipolis). MEG results were coregistered to DTI scans to provide Regions of Interest (ROIs) for evaluating tractography between those regions. Connections were found between sites of high coherence in each subject via major white matter fiber tracts. We conclude that MEG coherence analysis can be used to locate the zones of epileptform activity and DTI imaging can identify underlying connections between these interacting sites. These combined non-invasive modalities studies will lead to better understanding of epileptic propagation and networks.

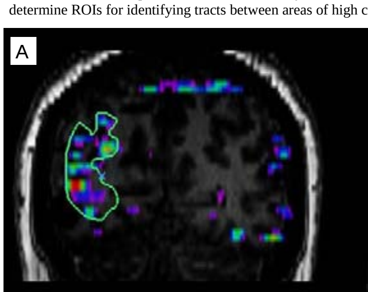
Introduction

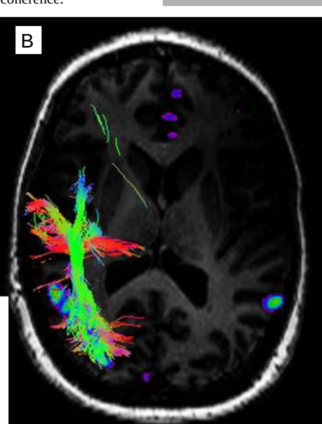
Synchronization of neuronal activity, characteristic of epileptic activity, can be quantified by coherence between cortical sites and calculated from non-invasive MEG imaged brain activation. Coherence analysis has been used in numerous studies to quantify spontaneous brain activity, including slow wave activity with both EEG and MEG. Coherence is a measure of the strength of functional interrelations between pairs of neocortical regions. Spontaneous brain activity can be recorded as transient waveforms and oscillations which can be quantified after transformation of the MEG data to the time frequency representation using short-time Fast Fourier Transform (FFT) analysis. After transformation, the strength of network interactions can be estimated by calculation of coherence to measure the synchrony between signals from different brain regions. High coherence sites are those participating in the epileptic network [1-5].

Diffusion is a random process resulting from the thermal translational motion of molecules. In a biological system, molecular diffusion is restricted by intra- and extracellular boundaries. DTI quantifies water molecule diffusion and also the degree and direction of anisotropy. Cerebral tissue has highly heterogeneous diffusion anisotropy due to regional differences in density of nerve fibers, concentrations of macromolecules and intracellular organelles, and density of myelination. Organized as bundles of axons and myelin sheaths running in parallel, white matter tracts can be deduced from anisotropy information. Tractography can be used to non-invasively identify pathways of major nerve fiber tracts as well as abnormalities in those tracts that cause disruption to the microstructural environment and subsequent reduction of anisotropy [6, 7].

Methods

- For 10 epilepsy patients, spontaneous MEG data was recorded for 10 minutes (sampled at 508 Hz, from 0.1 to100 Hz, forward and backward filtered using a 3-50 Hz bandpass) and divided into 7.5 second epochs.
- 148-channel Magnetometer MEG system (4D Neuroimaging Magnes WH2500)
- MR-FOCUSS-ICA was utilized to image the data. A sequence of FFT spectra were calculated (for every 0.5 s window within each epoch) for each ICA signal component and a coherence spectral matrix between sources was calculated for frequencies below 50 Hz.
- MEG data/results were coregistered to individual volumetric MRI scans.
- DTI scans were acquired (25 directions, 2.6 mm slices, b0=1000 s/mm^2, 3 Tesla, GE Scanner).
- DTI processing utilized MedINRIA (Copyright 2006 - Asclepios Research Project - http://www-sop.inria.fr/asclepios/) [8]. Tracking parameters were: Fractional Anistropy threshold 0.20, smoothness 0.20, minimum fiber length 0.10 mm.
- Each patient's volumetric MRI was coregistered to the b0 series images using ImageFusion (MedINRIA) utilizing a manual landmark transformation. The resulting transformation matrix was applied to the MEG results.
- MEG results were imported as functional overlays into the tracking program to determine ROIs for identifying tracts between areas of high coherence.





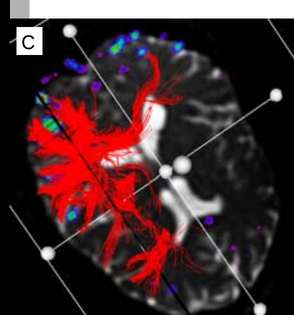


Figure 2. Imaged MEG Coherence of spontaneous cortical activity overlaid on the volumetric MRI of Patient # 9. Coherence scale of low to high is blue to red on the color scale.
A. Coronal view of the ROI surrounding the areas of high coherence in the right temporal lobe (green boundary line).
B. Superior axial view of resultant fibers are shown to include the Inferior Longitudinal Fasciculus (ILF) tracked through this single ROI outlining areas of high MEG coherence.
C. Inferior axial view of same fibers, colored red for visualization, illustrating connections to high MEG coherence areas.

Results

The coherence spectra identified epileptic network sites for each patient. MEG results, coregistered to the DTI scans, provided ROIs for evaluating tractography connections between those areas for each subject. The fiber connections between these ROIs were identified and compared to the major white matter fiber tracts for each subject. Major white matter tracts were identified utilizing the two ROI method established in DTI literature [9, 10]. **Table 1** lists the major connecting white matter fiber tracts that were identified to encompass the fibers linking the high coherence areas.

For an illustration of tract identification, see **Figure 1**. The areas of high MEG coherence of the underlying epileptic networks are presented for Patient 7. Light areas indicate high coherence and are shown as a functional overlay on the patient's volumetric MRI. Views **A** and **C** show fiber tracts identified by creating an ROI bounding the areas of high coherence in the right inferior parietal region. These fibers are shown in **A** from a superior view, which include Inferior Longitudinal Fasciculus (ILF) fibers as well as the forceps major (FM), the occipital projection of the callosal fibers. The callosal fibers provide pathways to the ipsilateral hemisphere and illustrate how network connections may propagate epileptic activity. The inferior view, **C**, clearly identifies the ILF. View **B** shows the ILF created using standard protocol tracking methods by choosing ROIs in temporal and occipital lobes [9].

A second example of the combined modalities imaging is shown in **Figure 2**. The areas of high coherence in the right temporal lobe of Patient # 9 are outlined in view **A**. This ROI was used to determine the fibers passing through this region of high MEG coherence then shown on the axial slice in view **B**. These fibers were identified as fibers from the right Inferior Longitudinal Fasciculus and connect with other areas of coherence shown an axial plane. This technique successfully identified fibers connecting MEG imaged areas of high coherence in all ten patients studied.

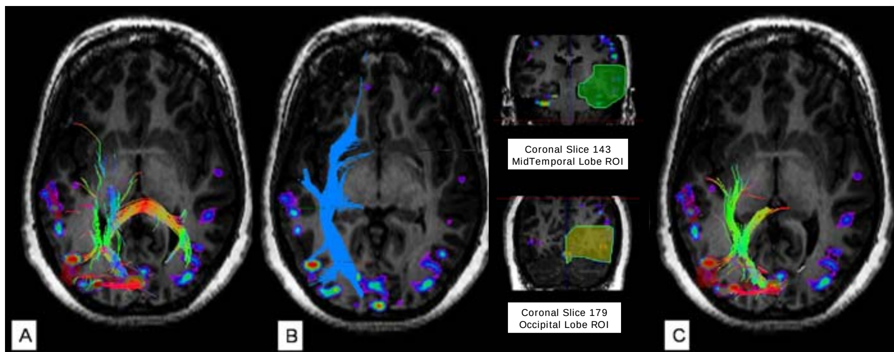


Figure 1. MEG imaged coherence of spontaneous cortical activity overlaid on the volumetric MRI of Patient # 7. Coherence scaling shown as low to high on blue to red color scale.
A. Superior view of fibers tracked from ROI bounding high coherence in right parietal lobe. All views are radiologic convention.
B. Inferior Longitudinal Fasciculus (ILF) tracked with the standard two ROI method between the MidTemporal and Occipital lobes shown inset [9, 10].
C. Inferior view of same fibers from view **A**. Areas of high coherence are linked with fibers from the ILF as well as occipital projections of the callosal fibers.

Table I. Summary of MEG Coherence & Connecting Tracts

ID	Areas of High MEG Coherence	Major Connecting Tracts*
1	R/L Inf Mot/Sen	CR
2	R Inf Mot/Sen, R Par	MCP
3	L Inf Par,R Par, R Inf Occ, L Inf Occ, R Occ	R/L IFO
4	L Temp, L Inf Front, L Par	ATR
5	R Mot/Sen, R Inf Par, L Inf Par, L Sup Par, L Sup Mot/Sen	MCP, PTR, STR, CR
6	R Temp, R Inf Occ, L Inf Occ	R IFO BA
7	R Inf Par, R Inf Temp, L Inf Temp	R IFO, ILF, FM
8	R Temp, R Inf Occ, L Temp, L Inf Occ	R&L IFO, ILF
9	R Inf Mot/Sen, R Inf Temp, L Inf Mot/Sen, L Inf Temp	R&L IFO, ILF, FM
10	R Inf Par, R Par, R Mot/Sens, R Sup Mot/Sen	R IFO, ILF, CR

*Key to Tract Abbreviations:
CR – Corona Radiation
FM – Forceps Major
IFO - Inf Fronto-occipital Fasciculus
ILF – Inferior Longitudinal Fasciculus
MCP – Medial Cerebellar Peduncle
PTR - Posterior Thalamic Radiation
STR - Superior Thalamic Radiation

Discussion

In the United States, approximately, 2.5 million people are diagnosed with epilepsy and 15 to 20 percent of these have seizures in spite of anticonvulsant therapy [11]. Epileptic network behavior has been shown to be associated with alterations in both gray and white matter in the brain [12]. In both ictal and interictal epileptic activity, abnormal transients and oscillations of brain electric activity are found in MEG and EEG of spontaneous brain activity. These transient waveforms and oscillations can be quantified and have been studied using coherence analysis to identify underlying network interactions.

Diffusion tensor imaging can uniquely deduce white matter tracts from anisotropy information. Several recent DTI studies have focused on temporal lobe epilepsy subjects suggesting degeneration of pathways with reduced fractional anisotropy (FA) [13, 14]. Comparison of ADC maps to epileptic zones identified with depth and subdural electrodes have shown increased diffusivity correlating with abnormalities [15, 16].

This study illustrates a technique to combine MEG and DTI imaging modalities to further understand the underlying networks in epilepsy patients. MEG coherence analysis identifies multiple brain regions that have significant interactions and may contribute to the propagation of epileptic activity. By using the MEG imaging results to determine regions of interest, we have compared the MEG identified tracts with those found using now standard two ROI techniques established in DTI literature. We have concluded that major fiber tracts connect areas of high MEG coherence in our subjects.

Conclusions

- MEG coherence analysis of spontaneous brain activity identifies active sites in epileptic networks.
- Areas of high MEG coherence can be used to define Regions of Interest for DTI imaging.
- Key white matter tracts that contribute to underlying networks in epilepsy subjects can be identified by combining MEG and DTI imaging.
- Future work will analyze tract properties and indices to determine possible abnormalities in the tracts identified with MEG coherence analysis.
- These combined modalities studies provide a powerful tool for studying the complex problem of understanding epilepsy.

References & Acknowledgement

1. Georgopoulos, Synchronous neural interactions assessed by magnetoencephalography: a functional biomarker for brain disorders. Journal of Neural Engineering, 2007. 4(4): p. 349 - 355.
2. David, Estimation of Neural Dynamics from MEG/EEG Cortical Current Density Maps: Application to the Reconstruction of Large-Scale Cortical Synchrony. IEEE Trans. on Biomedical Eng., 2002. 49(9): p. 975 – 987.
3. Gross, Dynamic imaging of coherence sources: Studying neural interactions in the human brain. PNAS, 2001. 98(2): p. 694-699.
4. Belardinelli, Localizing complex neural circuits with MEG data. Cogn. Process, 2006. 7: p. 53-59.
5. Bressler, Large-scale cortical networks and cognition. Brain Res Brain Res Rev, 1995. 20(3): p. 288-304.
6. Yogarajah, Diffusion-based magnetic resonance imaging and tractography in epilepsy. Epilepsia, 2007.
7. Rugg-Gunn, Diffusion imaging in epilepsy. Expert Rev Neurother, 2007. 7(8): p. 1043-54.
8. Toussaint, MedINRIA: DT-MRI Processing and Visualization Software, in in Proc. of MICCAI'07 Workshop on Interaction in Medical Image Analysis and Visualization. 2007: Brisbane, Australia
9. Mori, Imaging cortical association tracts in the human brain using diffusion-tensor-based axonal tracking. Magn Reson Med, 2002. 47(2): p. 215-23.
10. Wakana, Fiber Tract-based Atlas of Human White Matter Anatomy. Radiology, 2004. p. 77-87.
11. Kohrman, What is Epilepsy? Clinical Perspectives in the Diagnosis and Treatment. Journal of Clinical Neurophysiology, 2007. 24(2): p. 87-95.
12. Bernasconi, Whole-brain voxel-based statistical analysis of gray matter and white matter in temporal lobe epilepsy. NeuroImage, 2004. 23(2): p. 717-723.
13. Concha, Bilateral limbic diffusion abnormalities in unilateral temporal lobe epilepsy. Ann Neurol, 2005. 57(2): p. 188-96.
14. Gross, Extratemporal white matter abnormalities in mesial temporal lobe epilepsy demonstrated with diffusion tensor imaging. Epilepsia, 2006. 47(8): p. 1360-3.
15. Thivard, Interictal diffusion MRI in partial epilepsies explored with intracerebral electrodes. Brain, 2006. 129 (Pt 2): p. 375-85.
16. Guye, What is the significance of interictal water diffusion changes in frontal lobe epilepsies? NeuroImage, 2007. 35(1): p. 28-37.

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