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. Our 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) and processed using MedINRIA (Asclepios Research Project - INRIA Sophia Antipolis). MEG results were coregistered DTI scans to provide Regions of Interest 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 epileptiform 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.

KEYWORDS: MEG, DTI, epilepsy, fiber tracts, coherence

INTRODUCTION

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 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 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, divided into 7.5 second epochs then imaged using our MR-FOCUSS-ICA technique. 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, 3 Tesla, GE Scanner) and processed using 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. The volumetric MRIs were coregistered to the b0 images with ImageFusion (MedINRIA) utilizing a manual landmark transformation. The resulting transformation matrix was applied to the MEG results which were imported as functional overlays into the tracking program to determine Regions of Interest for identifying tracts between areas of high coherence.

RESULTS

The coherence spectra identified epileptic network sites for each patient. MEG results, coregistered to the DTI scans, provided Regions of Interest for evaluating tractography connections between those areas and are identified in Table 1 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.

Table I. Summary of MEG Coherence & Connecting Tracts.

ID	Areas of High MEG Coherence	Major Connecting Fiber 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
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 abbreviations: CR – Corona Radiation, FM – Forceps Major IFO - inferior fronto-occipital fasciculus, ILF – Inferior Longitudinal Fasiculus, MCP – Medial Cerebellular Peduncle, PTR - Posterior Thalamic Radiation, STR - Superior Thalamic Radiation

For an illustration of tract identification, see Figure 1. The areas of high MEG coherence of the underlying epileptic networks are presented for Subject 7. Light areas indicate high coherence and are shown as a functional overlay on the 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 Fasiculus (ILF) fibers as well as the forceps major, 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]. We compared major fiber tracks with those identified with the functional MEG analysis for each subject with results listed in Table 1.

A second example of the combined modalities imaging is shown in Figure 2. The areas of high coherence in the right

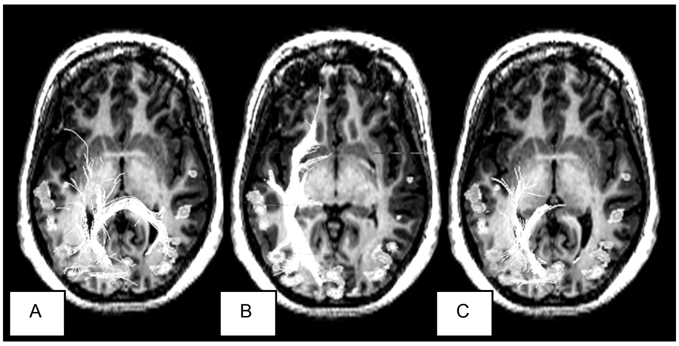

Fig 1. MEG Coherence of spontaneous cortical activity overlaid on the volumetric MRI of Subject # 7. Areas of coherence are overlaid in lighter shades. A. Superior view of fibers tracked from ROI bounding high coherence in right parietal lobe. B. Inferior Longitudinal Fasiculus tracked with the two ROI method between the temporal and occipital lobes. C. Inferior view of same fibers in view A. The areas of high coherence are linked with fibers from the ILF as well as occipital projections of the callosal fibers. Views are radiologic convention.

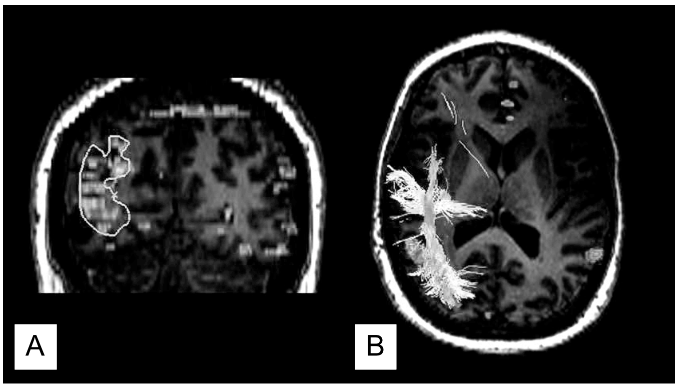

Fig 2. MEG Coherence of spontaneous cortical activity overlaid on the volumetric MRI of Subject # 9. High areas of coherence are lighter colored overlays. A. Coronal view of ROI surrounding high coherence areas in the right temporal lobe. B. Inferior Longitudinal Fasiculus fibers tracked through the single ROI identified from MEG coherence.

temporal lobe of Subject # 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 Fasiculus and connect with other areas of coherence shown in the axial plane. This technique successfully identified fibers connecting MEG imaged areas of high coherence in all ten subjects studied.

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 mulitiple 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.

CONCLUSION

Our results use MEG coherence analysis of spontaneous brain activity to identify key DTI imaged white matter tracts that contribute to underlying networks in epilepsy subjects. 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.

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