Preliminary Report on MEG Coherence Imaging Applications for Stroke

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Introduction

- New or recurrent stroke affects 700,000 people per year in the United States.
- Over 4 million Americans now live with the aftereffects of stroke.
- Most drug therapies for stroke focus on acute phase treatment (i.e. thrombolysis) or secondary stroke prevention.
  - These include thrombolysis, anticoagulant and antiplatelet drugs (aspirin), lipid lowering agents, and risk factor control.
- Recent experimental studies on functional recovery in animal models after stroke, have focused on the use of pharmacological treatments
  - Sildenafil citrate (Viagra), erythropietin (EPO), and statins, which have shown promising neurogenesis results.
  - Some of these treatments are now in clinical trials at Henry Ford Hospital (HFH) and elsewhere.

Scientific Problem

- No precise imaging tool providing evidence that stroke treatments will improve neurological and functional outcomes.
- Neurological outcome is measured by The National Institutes of Health Stroke Scale (NIHSS).
  - Standardized and validated clinical instrument that assesses severity of neurological impairment after stroke.
  - NIHSS is not an imaging technique or a histological assessment, but a subjective grading of a subject's ability to perform functional tasks such as movements of the legs, arms, and fingers, level of consciousness, eye gaze, ability to talk, extinction and inattention are also measured.
- The current challenge is to determine functional imaging methods to identify recovery-related therapeutic targets and prognostic factors for gauging stroke recovery and effectiveness of medical treatments.
  - Tecchio, 2007 has reported that delta band power in the unaffected hemisphere measured by MEG has a negative corellation with recovery from stroke.

Hypothesis

- MEG can be used to diagnostically detect neurologic damage and recovery after stroke.
- Abnormal MEG and EEG slow waves have been observed in the vicinity of structural lesions usually generated around the penumbra of the stroke lesion.
- Coherence mapping of spontaneous MEG can determine the neuronal network disruptions detected within the first four weeks of a stroke.
- Serial coherence mapping studies of spontaneous MEG can detect neuronal restoration or realignment of cortical networks one to six months after a stroke.

Extracting Real-time Neural Networks from MEG data

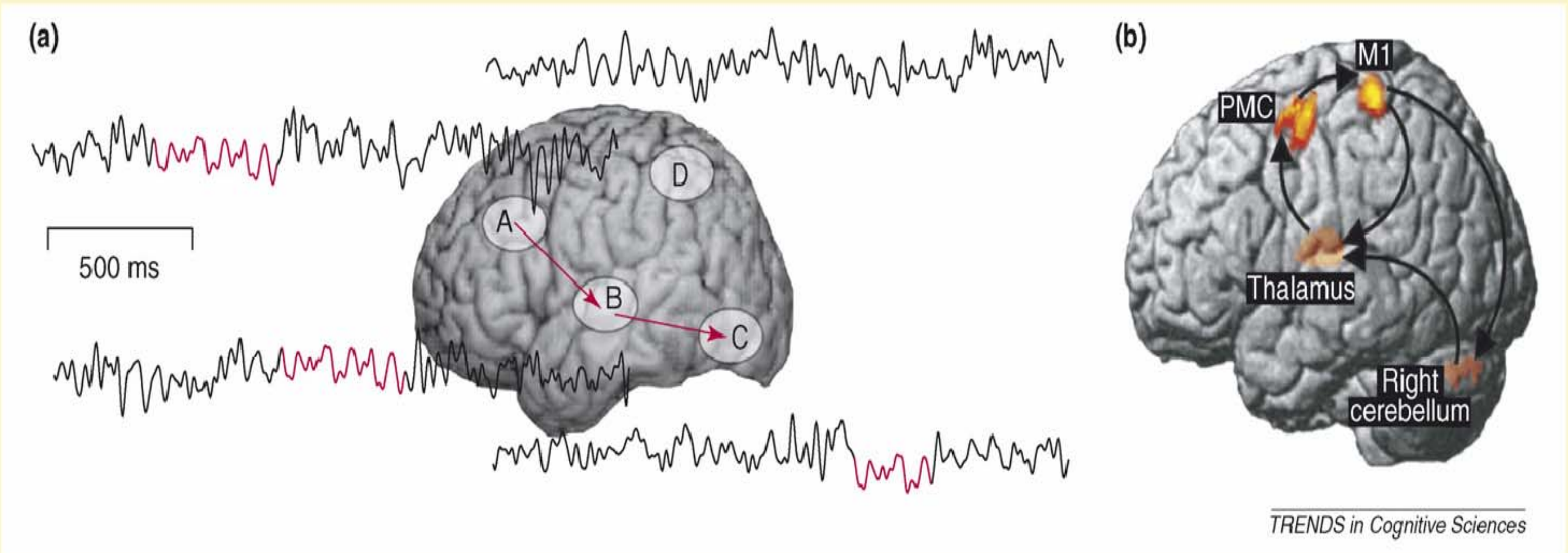


Figure I. Extracting long-range neural connectivity from MEG data. **(a)** Simplified presentation of the basic idea. Curves depict time courses of activity in four brain areas (gray ellipses). If neuronal populations in these areas are functionally connected, one would expect to detect similar time courses of activation in the different areas (red segments), at least occasionally. Time shifts between similar stretches of activity could be interpreted as flow of information. In this example, one could argue that there is a drive from area A to B and a weaker drive further to area C. Delays between the repeated segments are exaggerated. **(b)** Neural network during slow movements of the right index finger. Here, EMG from the moving finger provided a meaningful, nonbrain reference signal. EMG–MEG coherence led to the contralateral motor cortex, which served as a reference area for identification of the network within the brain. Abbreviations: M1, primary motor cortex; PMC, premotor cortex. Reproduced, with permission, from Ref. [48].

Gross J, et al Proc Natl, Acad Sci. 2002

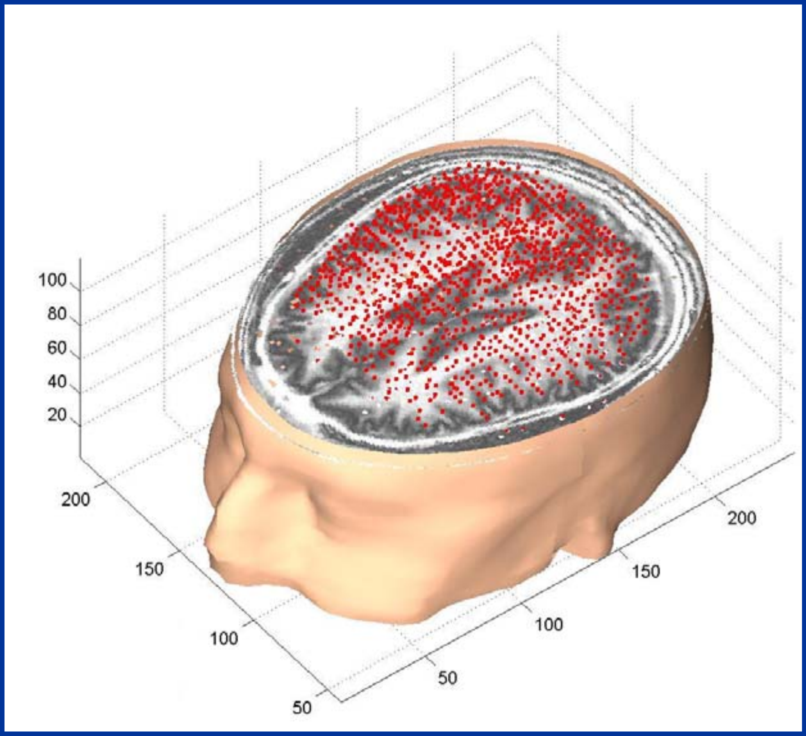
Coherence Imaging: Calculation

1. Calculate time sequence of brain activity
   a. ICA extraction of burst activity brain source signals
   b. MR-FOCUSS (current density) imaging of ICA components
2. Calculate FFT sequence
3. Calculate cross-spectral matrix between sources by multiplying the Fourier-transformed signals (frequency space) of the time series.
4. Calculate coherence matrix by normalizing the cross spectral density with the power spectral density of both time series. Its values ranges from 0 (no similarity) to 1 (identical time series).
5. Calculate average coherence, each source

Methods

- 10 patients who had a diagnosis of a recent cerebral infarct studied by MEG.
  - 3 patients have had one MEG scan
  - 5 patients have had 2 MEG scans
  - 1 patient has had 3 MEG scans
  - 1 patient has had 4 MEG scans
- 2 control subjects each have had 2 MEG scans
  - 148 channel MEG system (4D-Neuroimaging Magnes WH2500)
  - Spontaneous cortical brain activity recorded for 18 minutes.
  - Sampling rate 254Hz,
  - Bandpass DC-100Hz
  - Data filtered from 1-7 Hz, 7-15 Hz, 15-25 Hz and 25-50 Hz
  - Analyzed in MR-FOCUSS, a current density analysis technique capable of imaging simultaneous activity in multiple cortical structures and correlating with specific anatomical structures in the volumetric MRI.
  - Coherence analysis was then performed and compared to the location of the lesion from the recent stroke.

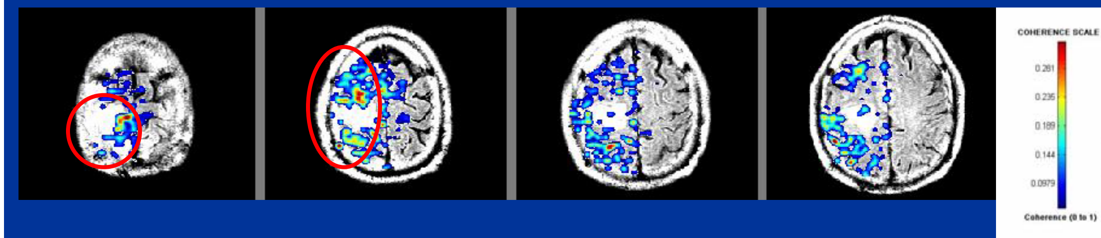
MR-FOCUSS Cortical Model



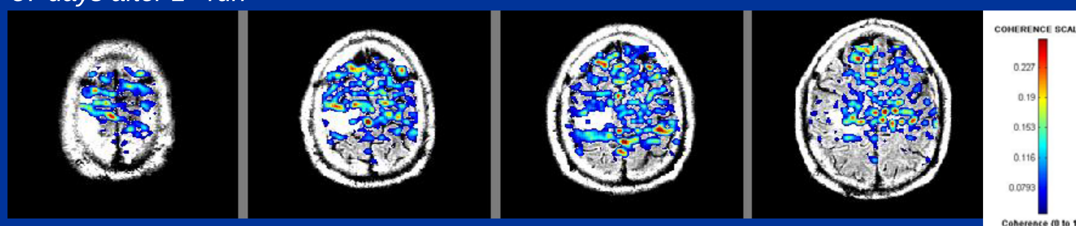
- Created from Volumetric MRI Data
- ~4,000 cortical locations
- 3 dipoles at each location that represent x, y, z
- Distribution matches cortical gray matter

Coherence changes in Delta/Theta (1-7Hz) Patient 4514

1st Run with in 72 hours of stroke



57 days after 1st run



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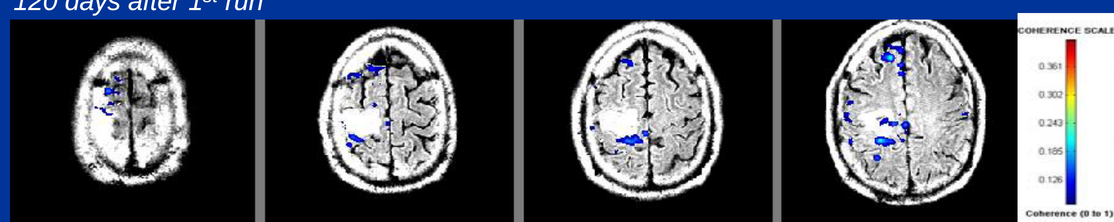
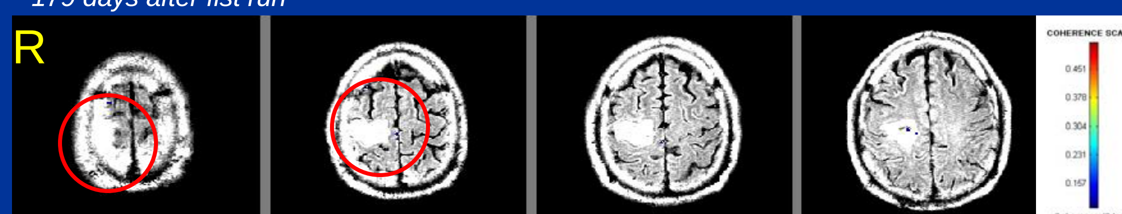
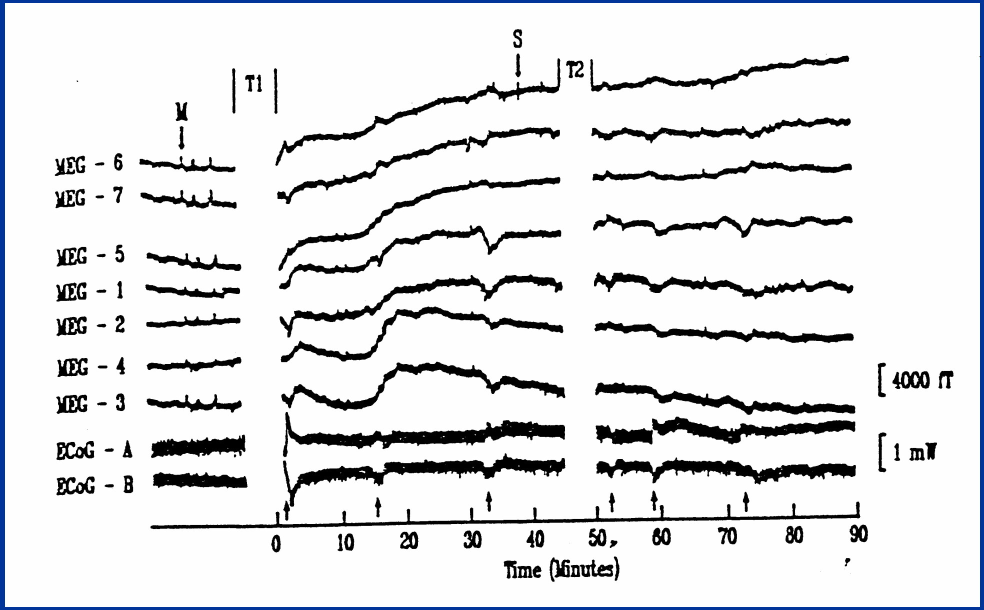


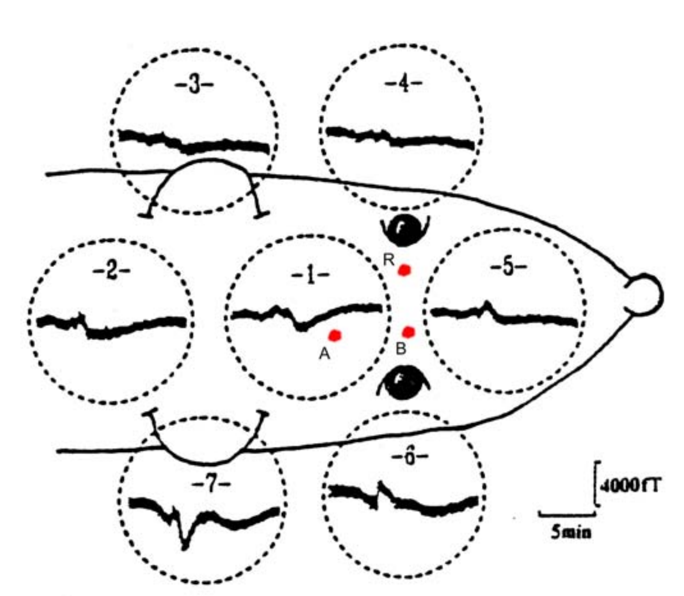
179 days after fist run



Delta/Theta Coherence and SCD

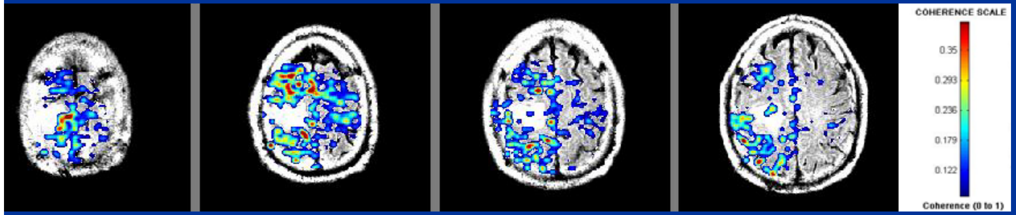
- Stroke/ischemia: SCD-like phenomena are associated with peri infarct depolarizations that surround and radiate from ischemic lesions (Hossman, 1996).
- Chen et al showed DC MEG could detect SCD during MCA occlusion in Rat model (Stroke, 23: 1299-1303, 1992).
- Early ipsilateral Delta/theta coherence is likely do to this process





Coherence changes in Alpha (7-15Hz) Patient 4514

1st Run with in 72 hours of stroke



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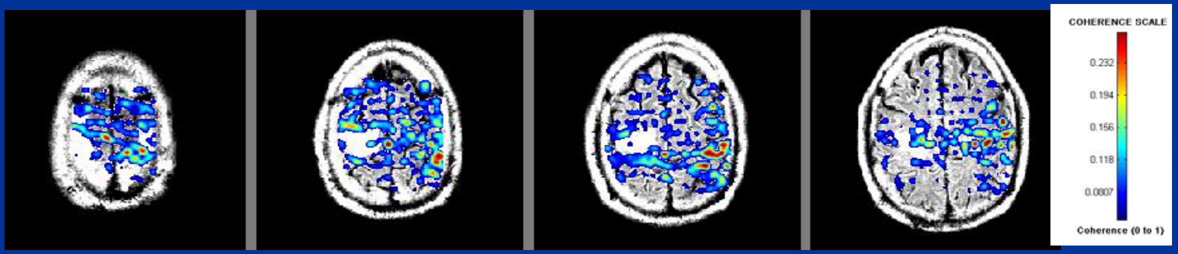

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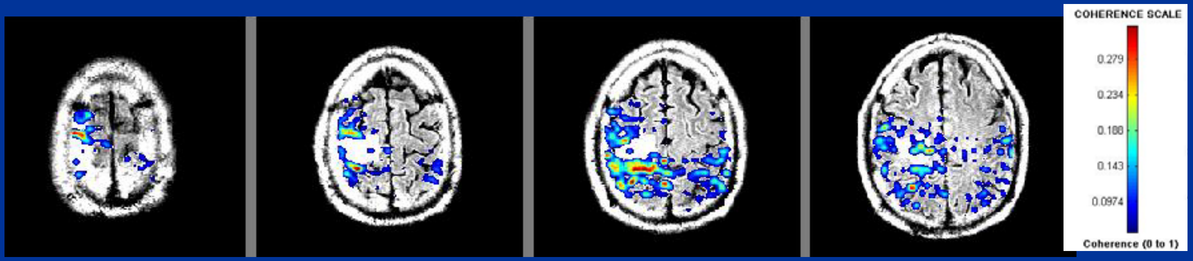

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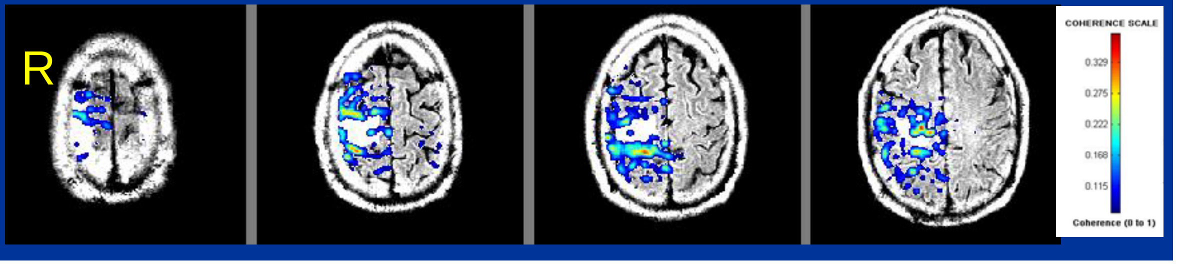
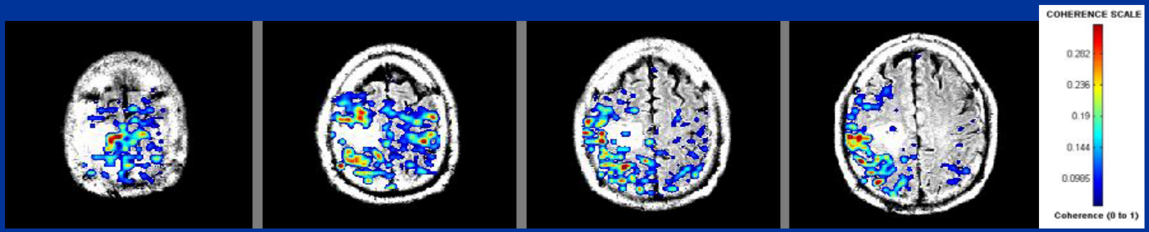


Coherence changes in Beta (15-25Hz) Patient 4514

1st Run



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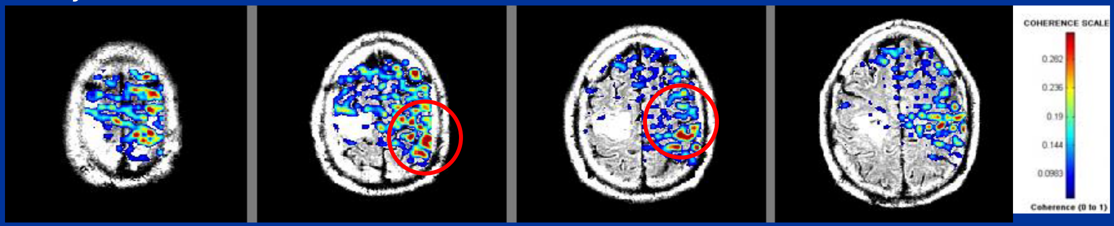

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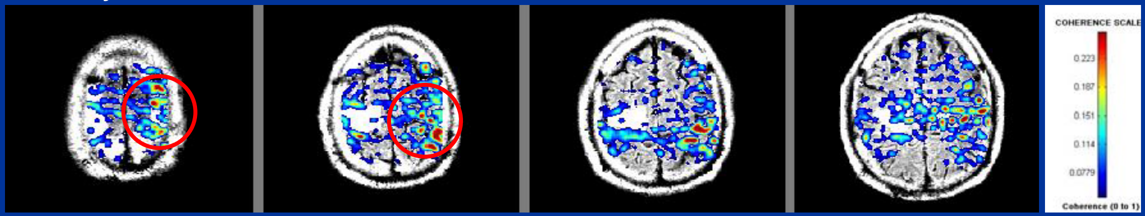

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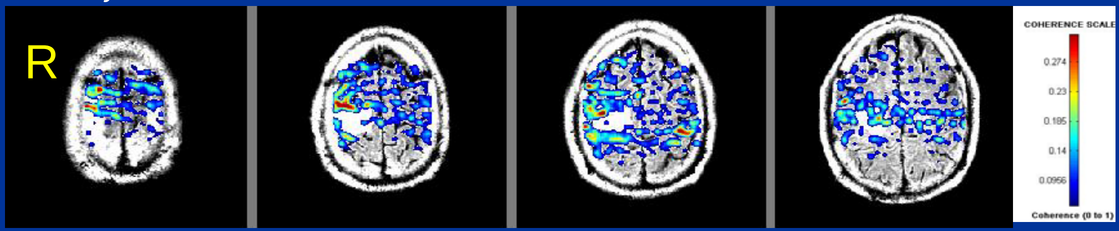
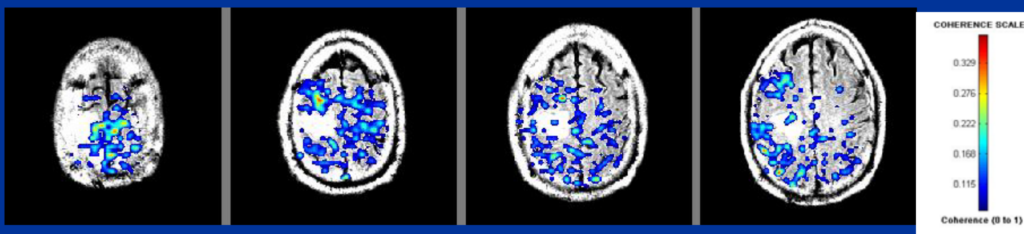


Coherence changes in Gamma (25-50Hz) Patient 4514

1st Run



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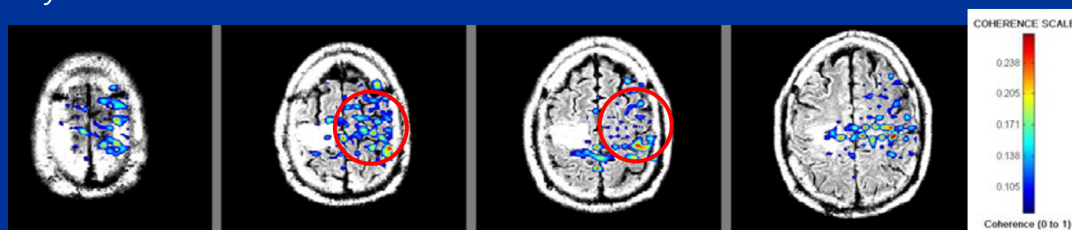

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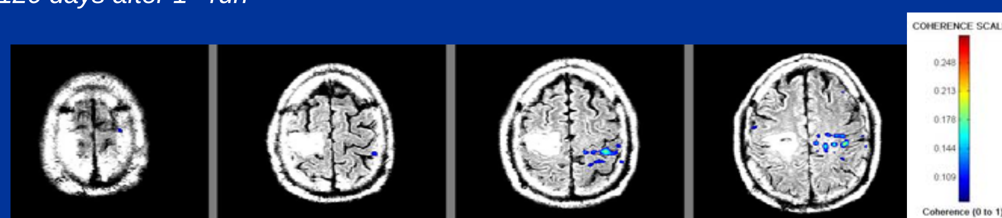

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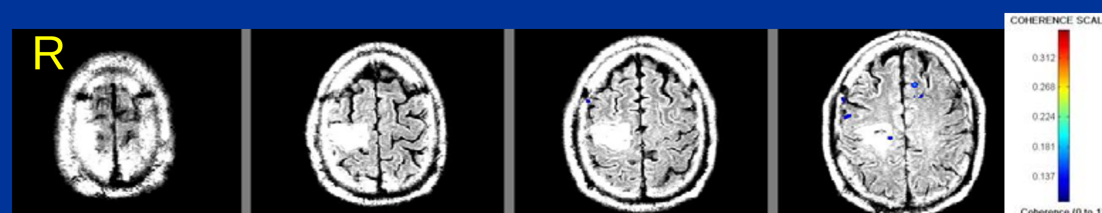

Results

- In stroke patients, as has been known since the studies of Gray Walter in EEG in the 1950s, the lower frequencies of 1-7Hz represent the breakdown of networks between neurons, a process that is accompanied by anoxic depolarization (Hossman, 1996)
- Coherence measurements in serial spontaneous MEG recordings reveals a dynamic process that follows a different time course in the various frequency bands.
  - In the delta/theta range, increased coherence was seen surrounding the lesion was seen in the first few days after the stroke (in 7 subjects with lesions) and continued for weeks.
  - The delta/theta coherence lessened over time with subsequent scans.
- In the initial MEG scans,15-25 Hz beta band coherence was seen surrounding the lesion.
  - After 4 weeks, the MEG imaged regions on the contralateral hemisphere showed beta frequency coherence in the similar mirror area of the lesion
  - In the most extensively studied patient so far, this activity lasted for approximately 3 months.

Preliminary impressions from our ongoing study

- Coherence mapping of spontaneous MEG shows serial changes at different frequency bands following stroke.
- Coherence mapping can be used to study the sequence of neurophysiological changes occurring after stroke.
- In our preliminary study, ipsilateral low frequency activity dominates acutely but diminishes over time.
- High frequency activity presents a more complex picture. Some patients have shown ipsilateral beta frequency coherence acutely but in general, beta and gamma frequency coherence is present contralateral to the side of the infarction.
  - Is coherence in the faster frequency bands a measure of increased synaptic plasticity mediated by glutamate transmission similar to the recent work of Centonze et al, 2007?
  - Is there prognostic significance in any of the coherence data since increased excitatory activity has been shown to be beneficial or detrimental depending upon where it occurs relative to the ischemic penumbra and whether it is ipsilateral or contralateral to the site of the lesion?
- If so, coherence imaging may provide physicians with MEG markers or factors to identify recovery-related neuronal events to determine the course of treatment for stroke.

Acknowlegment

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MEG_TOOLS

a complete MEG analysis software package (requires Matlab)

available at www.megimaging.com