MEG Study of Stroke Recovery

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Abstract

Objective: This study utilized MEG to detect neurological damage and recovery after stroke.

Methods: We recruited 11 patients who had recent strokes and 5 control subjects for comparison. Spontaneous cortical brain activity was recorded with MEG for 18 minutes. Data were sampled at 254Hz, DC-100 Hz, filtered from 1-7, 7-15, 15-25 and 25-50 Hz and imaged with MR-FOCUS. Coherence analysis was then performed and compared to the location of the stroke lesion.

Results: In stroke patients, coherence in the delta frequencies (1-7 Hz), known to represent the breakdown of networks between neurons [1], was seen 2 days after stroke, in the lesion penumbra, and continued for 5 weeks. These delta frequencies lessened over time with subsequent scans. The higher frequency activity is known to represent axonal sprouting and restoration [2]. On the initial MEG scan, 15-25 Hz activity was seen surrounding each patient's lesion. After 4 weeks, regions in the contralateral hemisphere showed coherence in the mirror area of the lesion, suggesting that the contralateral hemisphere began assuming limited function previously demonstrated by the lesion area. This activity lasted for ~ 3 months. In control subjects scattered brain regions of coherence were imaged but none of these areas were consistently imaged over time.

Conclusion: This study confirmed that MEG can determine the status of recovering coherence in neuronal networks after stroke. Delta activity gradually diminishes with time and is replaced by higher frequencies in the contralateral region. Coherence imaging may provide physicians with MEG markers to identify recovery-related neuronal events which could determine the course of treatment after stroke. These studies may also further the basic science of the underlying neural networks involved in stroke.

Methods

- 11 patients with diagnoses of recent ischemic strokes were recruited. 4 patients did not return for further MEG scanning. Of the remaining patients, 5 had two scans, 1 had three scans, and 1 had four scans.
- The study population included 8 men and 3 women. Mean age was 51 years (range 29-69).
- 10 patients presented with ischemic and one presented with hemorrhagic stroke.
- Stroke location was brainstem in 1, subcortical hemispheric in 4, and cortical in 6 patients.
- Median NIHSS* at the time of the initial scan was 4 (range 1-22).
- MEG scanning was performed at a mean of 4 days post-onset of stroke, and then, at 60, 120 and 180 days.
- These patients were compared with 5 control subjects who had two scans each separated by 4 weeks.
- 148-channel MEG system: Magnetometers (4D Neuroimaging Magnes WH2500) recorded spontaneous cortical brain activity for 18 minutes.
- Data were sampled at 254Hz, DC-100Hz.
- Data were separated into 4 separate frequency filtered bands: 1-7 Hz Delta/Theta, 7-15 Hz Alpha, 15-25 Hz Beta, and 25-50 Hz Gamma.
- MEG data were analyzed with MR-FOCUSS, a current density analysis technique capable of imaging simultaneous activity in multiple cortical structures and correlating with specific anatomical structures on volumetric MRI [3].
- Coherence analysis was performed on the imaged MR-FOCUSS MEG results and compared to lesion location on MRI [4].

NIH Stroke Scale (NIHSS)

*The NIHSS scale is a quantified neurological examination with 11 elements assessing consciousness, eye movement, vision, facial strength, limb strength, coordination, sensation, language, speech clarity, and spatial attention. Scores range from 0 – 38 with 0 being normal and higher scores indicating decreased neurological function. The exam takes approximately 5-10 minutes to complete.

Introduction

New or recurrent stroke affects 700,000 people per year in the United States [5]. Over 4 million Americans now live with the aftereffects of stroke [5]. Most drug therapies for stroke focus on acute treatment (i.e. thrombolysis) or secondary stroke prevention. Recent experimental studies on functional recovery after stroke have concentrated on the use of pharmacological treatments which have shown promise in neuronal and vascular remodeling. Some of these treatments are now in phaseI/II studies.

Presently no precise imaging tool provides evidence of treatment induced neurogenesis in stroke patients or signals changes correlated with outcome. The neurological outcome for a stroke patient is measured by his/her score on the National Institutes of Health Stroke Scale (NIHSS). This is not an imaging technique or histological assessment, but a clinical grading of the ability to perform functional tasks such as, movements of legs and arms, eye gaze, level of consciousness, ability to talk, and attention to spatial orientation. Functional imaging measurements of stroke would be clinically useful as a tool for gauging stroke recovery and effectiveness of medical treatments. The current challenge is determining methods to identify recovery-related therapeutic targets and imaging prognostic factors [6].

In this study we used MEG coherence imaging for estimating cortical connectivity to evaluate the integrity of a stroke patient's cortical network. Recently, techniques have been investigated that calculate coherence between sources of MEG imaged brain activity. These techniques vary in analysis methods applied to MEG data, the number of sources for which paired coherence can be calculated, and the use of phase synchrony in place of coherence. MR-FOCUSS is capable of imaging both focal and extended cortical activation [3]. We have combined MR-FOCUSS with Independent Component Analysis (ICA) that enhances the imaging of brain electric activity [4]. We investigated the utility of MEG for detecting neuronal changes indicative of brain repair in the cortex after stroke. The extent and severity of neuronal damage may correlate with recovery or failure thereof. MEG has the potential for defining functional outcome after stroke and enhancing existing prognostic indicators (NIHSS & MRI).

Results

• Coherent brain activity in the Delta range (1-7Hz), surrounding the lesion, was seen three days after stroke and continued with no significant change through the second scan (Fig 1). Across all time points the average correlation coefficient for run to run coherence was r=0.77±0.09, 95% confidence limits. Between day 57 and day 120 as the delta band resolved, the coherence was significantly reduced, r=0.565±0.02, as compared with the run to run correlation. These lower frequencies correlate with breakdowns in the neuronal networks [1]. Delta frequencies diminished by 180 days in patients who experienced good outcome.

• On initial MEG scans, Beta (15-25Hz) activity was seen around the lesion (Fig 2). Higher frequency activity is correlated with axonal sprouting and restoration [2]. After 4 weeks, the contralateral hemisphere showed Beta coherence in a mirror area to the lesion; activity lasted for nearly three months. Changes in the Beta coherence was significant between the 57, 120 and 179 day time points (r=0.69±0.02 and r=0.65±0.02).

•Coherent Alpha band brain activity (7-15 Hz) was continuously active over the entire interval (Fig 3). There were no significant activations in any patient that correlated with outcome.

•At 8 weeks Gamma band (25-50Hz) activity mirrors the area of the lesion (Fig. 4).

Figures

Delta/Theta (1-7)

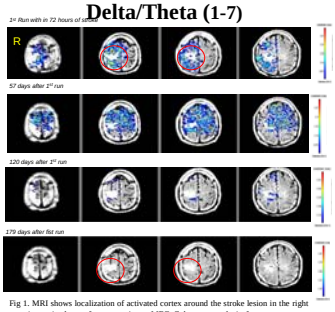


Fig 1. MRI shows localization of activated cortex around the stroke lesion in the right superior parietal area for one patient. MEG Coherence analysis from spontaneous brain activity is shown on the MRI. Circles indicate cortical areas where significant changes in Delta coherent activity occurred. This patient had a good outcome.

Beta (15-25Hz)

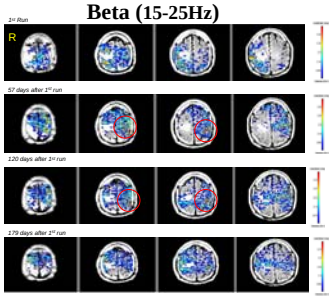


Fig 2. MEG Coherence analysis for the Beta range brain activity from same patient as shown in fig 1. Circles show Beta activity is seen in the contralateral hemisphere starting at 4 weeks after stroke and continuing for 4 months.

Alpha (7- 15 Hz)

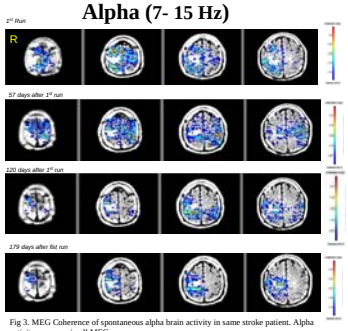
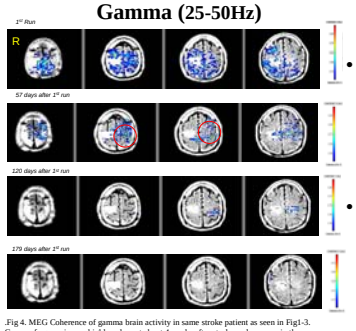


Fig 3. MEG Coherence of spontaneous alpha brain activity in same stroke patient. Alpha activity was seen in all MEG scans.

Gamma (25-50Hz)



.Fig 4. MEG Coherence of gamma brain activity in same stroke patient as seen in Fig1-3. Gamma frequencies are highly coherent about 4 weeks after stroke and are seen in the contralateral hemisphere.

Conclusions

- This study of human patients with recent ischemic stroke shows that slow frequencies on MEG gradually diminish with time and are replaced by higher frequencies in the contralateral region when the patient experienced a good or positive outcome.
- We have shown that MEG can non-invasively determine the status of recovering coherence in neuronal networks after a stroke.
- Further studies with MEG may elucidate the basic mechanisms under underlying neural network recovery after ischemic stroke.
- Studies, such as these, may lead to prognostic techniques for evaluating stroke patients.

References and Acknowledgment

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Discussion

- Imaging the magnetic fields arising from stroke patients may lead to prognostic indicators of recovery for clinical application.
- Changes in low frequency neuronal activation after drug therapy may help in determining drug effectiveness in restoring brain function.
- Further studies will investigate whether MEG can detect brain activity changes after stroke and provide clinicians with a tool for gauging stroke recovery and treatment efficacy.
- MEG may emerge as an imaging modality, useful in the early indications of good recovery or treatment.
- This study may help establish MEG analysis as a biomarker for determining the prognosis for recovery after stroke, and add information to existing prognostic indicators (NIH stroke scale and MRI).