QUANTITATIVE ELECTROENCEPHALOGRAPHY IN A PATIENT EMERGED FROM THE MINIMALLY CONSCIOUS STATE AFTER 19 YEARS

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334.21

INTRODUCTION

The minimally conscious state (MCS) is characterized by reliable but inconsistent behavioral evidence of self or environmental awareness. Recent studies show that time in MCS is not well-correlated with functional recovery complicating efforts to provide an accurate prognosis (cf. Lammi et al. 2005). Very late recoveries from MCS, though rare, are documented. Although clinical examination may suggest residual cognitive function, there are no functional imaging or electrophysiological measurements to unequivocally assay cognition in MCS or to predict recovery.

Goals of the study:
This is a pilot study using functional electroencephalography (EEG) methods on a patient who emerged from MCS to further understand patterns of recovery from MCS and to find markers for recovery after brain injury. This study is related to a prior study (*Schiff et al 2005*) using the same auditory stimulus paradigm in MCS patients, but with functional magnetic resonance imaging (fMRI) as the neuroimaging technique. The goal is to determine if measurements of EEG coherence and power spectra can be complementary to fMRI in documenting neural activity and connectivity under different conditions and to ultimately correlate these results with anatomical and functional imaging findings (structural MRI, diffusion tensor MRI, functional MRI and positron emission tomography (PET)).

METHODS

Subjects and experimental conditions:
We recorded continuous EEG using the standard 10-20 electrode placement system (recorded with Xltek software www.xltek.com) from a 40 year-old male patient who unexpectedly emerged from MCS after 19 years. The patient suffered traumatic brain injury at age 19 during a motor vehicle accident. He spent approximately 6 weeks in coma followed by brief a period in the vegetative state, then a 19 year period exhibiting minimal interaction with his environment until he spontaneously began to regain language function during June of 2003. At the time of this study, he was able to speak in full sentences, although he was limited by poor short term memory and an inability to move all extremities except for his right arm.

To examine language responsive network functions we calculated EEG power spectra and coherence during 3 conditions:
- the subject listened to a recorded narrative spoken by his mother containing personally meaningful content ("**forward**")
- the same narrative played time-reversed so they were recognizable as speech but without content, propositional or prosodic information ("**backward**")
- during a period of time without playing the recorded narrative ("**silence**")

EEG was also recorded from a normal subject (*Normal)* during the same 3 conditions using a 128 lead electrode net (Electrical Geodesics www.egi.com) and recorded using Net Station (www.egi.com/netstation).

Data analysis:
EEG signals were reviewed for artifacts, and data recorded from electrodes with persistent artifacts were not analyzed. This resulted in the removal of all EEG data recorded from the frontal leads for the patient and also the data recorded from the occipital and some of the temporal leads for the normal subject.

Artifact-free data were selected and grouped together according to the auditory stimulation condition. We examined power spectra at frequencies ranging from 0 to 100Hz for each EEG channel (displayed up to 50Hz on this poster). We computed coherence spectra for each of the leads with their nearest intrahemispheric neighbor, as well as for interhemispheric pairs of leads.

Power spectra summarize the frequency content of the time-varying EEG signal and index the relative strength of contribution of particular frequencies to the overall composite signal.

The *coherence* of two signals provides a measure of cross-correlation in the frequency domain and can be thought of as an index of dynamic interaction of two signals at particular frequencies (Bendat and Piersol, 2000). The coherence is computed from the cross spectrum at a given frequency *f* normalized by the power spectra of each signal (using the square root of the sum of their squares, see Eq. 6 below). Thus obtaining peaks or dips in the coherence is not simply the result of a strong peak in a frequency range of one or the other power spectra (see adjacent poster 334.20, panel for Patient 1 showing the F4-T4 coherence and explanation for example).

Power and coherence spectra were computed using multi-taper methods (Thomson and Chave 1991, Mitra and Pesaren 1999) on 1 second swatches of data sampled at 200 Hz for the patient data and 250 Hz for the normal subject data. Three Slepian data tapers were used for the power spectra computation to obtain a frequency resolution of 4 Hz and 10 Slepian data tapers were used for the coherence spectra providing a frequency resolution of 11 Hz.

The multi-taper method is based on the use of multiple orthogonal data tapers to stabilize the variance and optimize the bias of a spectral estimate. A direct estimate of the power spectrum, $S_{MT}(f)$ (see Eq. 2), is calculated using this method by averaging over individual tapered spectral estimates , where

$$\tilde{x}_k(f) = \sum_{1}^{N} w_t(k) x_t \exp(-2\pi i f t) \tag{1}$$

The weights w_t represent the sequence of orthogonal data tapers, x_t is the signal. The estimate of the power spectrum is obtained by averaging over the tapered estimates:

$$S_{MT}(f) = \frac{1}{K}\sum_{k=1}^{K}\left|\tilde{x}_k(f)^2\right| \tag{2}$$

The coherence spectrum, *C*(*f*), is similarly obtained from multi-taper estimates of the power spectra from two signals (S^1 and S^2 , see Eq. 6 below). To calculate confidence limits for our power spectra and coherence we use jackknife methods as developed by Thomson and Chave (1991). The logarithm of the power spectrum at a single frequency is used to stabilize the estimation procedure. Delete-one jackknife estimates are formed as in (3) and their average (4) to obtain a spectrum estimate. The jackknife estimate of the variance of the log power spectrum is given by (5). Using these quantities it is possible to construct confidence intervals for the power spectra and coherence estimates shown on the poster (see Thomson and Chave 1991). Coherence estimates at a frequency *f* are computed as shown in Eq. 6.

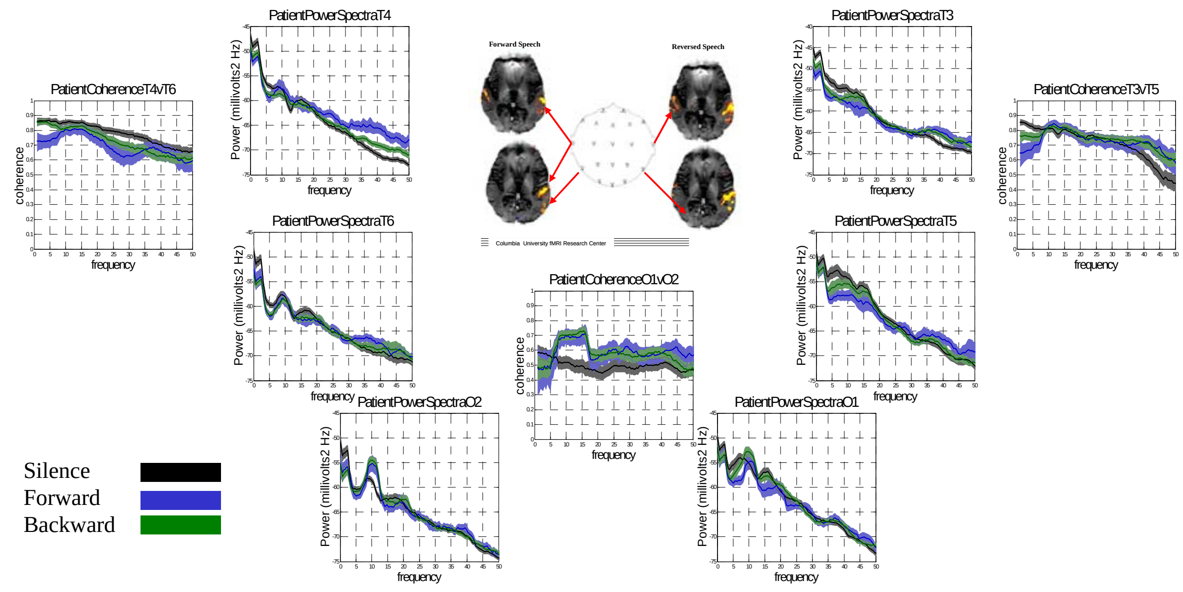
$$\ln \hat{S}_{\hat{j}} = \ln\left(\frac{1}{N-1}\sum_{\substack{i=1,\\ i\neq j}}^{N}\hat{S}_i\right) \tag{3}$$

$$\ln \hat{S}_{\cdot} = \ln\left(\frac{1}{N-1}\sum_{\substack{i=1,\\ i\neq j}}^{N}\hat{S}_{\hat{j}}\right) \tag{4}$$

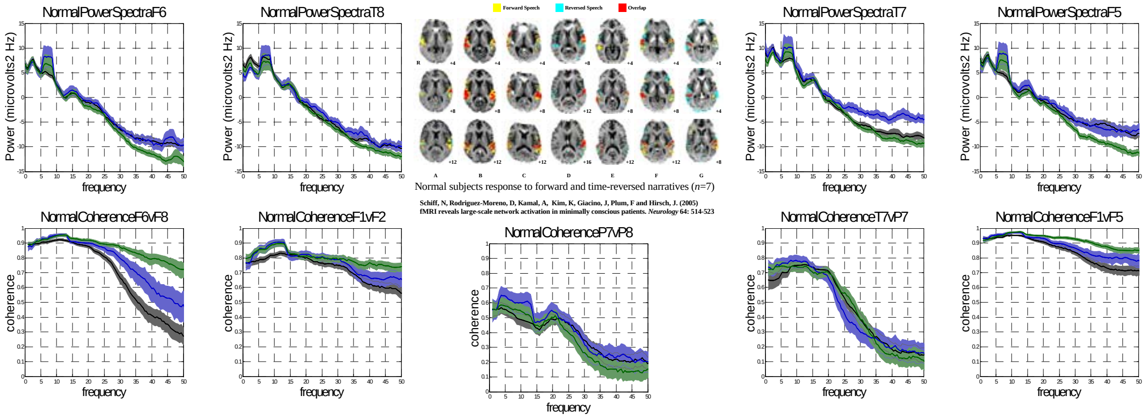
$$\hat{\sigma}^2 = \mathrm{var}\{\ln \hat{S}\} = \frac{N-1}{N}\sum_{i=1}^{N}(\ln \hat{S}_{\hat{j}} - \ln \hat{S}_{\cdot})^2 \tag{5}$$

$$\hat{C}_{\hat{j}}(f) = \frac{\sum_{\substack{i=1,\\ i\neq j}}^{N}\hat{S}_i^1(f)\hat{S}_i^2(f)}{\sum_{\substack{i=1,\\ i\neq j}}^{N}\left|\hat{S}_i^1(f)\right|^2\sum_{\substack{i=1,\\ i\neq j}}^{N}\left|\hat{S}_i^2(f)\right|^2} \tag{6}$$

Patient EEG Power and Coherence Spectra and fMRI during silence and while listening to narrative played forward and time-reversed



Normal EEG Power and Coherence Spectra and fMRI during silence and while listening to narrative played forward and time-reversed

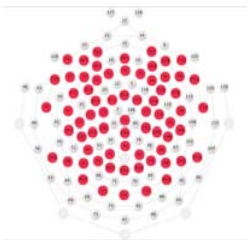


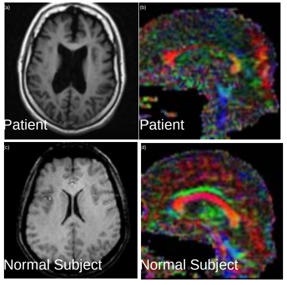
Normal subjects response to forward and time-reversed narratives (*n*=7)

Schiff, N, Rodriguez-Moreno, D, Kamal, A, Kim, K, Giacino, J, Plum, F and Hirsch, J. (2005) fMRI reveals large-scale network activation in minimally conscious patients. *Neurology* 64: 514-523

Anatomic and Diffusion Tensor Imaging

EEG Locations for Normal Subject





Average Coherence Values For All Conditions At Each Frequency Range For Patient and Normal

Normal

Comparison	0 to 7	8 to 14	15 to 30	31 to 50
C1vC3	0.75	0.9	0.9	0.8
C2vC4	0.6	0.8	0.82	0.7
C3vC4	0.15	0.1	0.08	0.2
C3vP3	0.8	0.9	0.85	0.75
C5vT7	0.8	0.8	0.7	0.2
C4vP4	0.7	0.75	0.78	0.55
P4vP3	0.4	0.3	0.4	0.25
P3vP7	0.8	0.85	0.85	0.8
P4vP10	0.8	0.8	0.8	0.7
T7vP7	0.7	0.75	0.6	0.2

Patient

Comparison	0 to 7	8 to 14	15 to 30	31 to 50
C3vCz	0.4	0.5	0.55	0.35
C4vCz	0.55	0.6	0.7	0.75
C3vC4	0.1	0.1	0.2	0.25
C3vP3	0.7	0.65	0.6	0.75
C3vT3	0.75	0.75	0.6	0.5
C4vP4	0.65	0.7	0.65	0.7
P3vP4	0.3	0.2	0.25	0.3
P3vT5	0.7	0.8	0.7	0.8
P4vT6	0.7	0.8	0.8	0.75
T3vT5	0.75	0.8	0.75	0.65

SUMMARY AND CONCLUSIONS

We used EEG power spectra and coherence analysis of neighboring and interhemispheric electrodes to study the brain of a patient who emerged from a 19 year minimally conscious state after traumatic brain injury, and compared the results to the patients fMRI and anatomical MRI data as well as a normal control. EEG was recorded while subjects listened to a spoken narrative played forward and in time reverse as well as during silence.

1. The patient has similar amounts of coherence as a normal subject (see table). This is despite the severe brain injury the patient underwent resulting in loss of much of his white matter (as seen on the diffusion tensor MRI).

2. During the listening tasks, the patient's power spectrum of his temporal lobe EEG has suppression of activity in the lower frequencies but increase in power in the higher frequencies. These findings seem to correlate with increased activity in these regions on the patient's fMRI. Coherence spectra between ipsilateral temporal leads show a similar frequency distribution of difference on the left side possibly reflecting increase language activation on the left side as seen on fMRI. In the normal there is increase power while listening to the language condition in the left temporal lobe only. It is impossible to fully interpret the findings in the normal since most temporal leads were not analyzable due to artifact.

3. In the normal subject's frontal lobe there is increased coherence at low and high frequencies during the listening tasks. This may reflect increased frontal lobe activity during these tasks.

4. There is increased power and coherence in the patient's occipital lobe during the passive listening condition around 10 Hz. This increase in low frequency activity may reflect decreased activity in that region. This could not be confirmed in the normal due to artifact though a similar finding is seen in the interparietal lobe coherence.

These findings may be representing processing of language stimuli and reflect return of full consciousness. The study is limited by artifact in many leads not allowing study of the patient's frontal lobe and normal's occipital and many temporal leads. If these findings can be replicated in other subjects, they may be useful to use on patients with disorders of consciousness to determine patients level of consciousness and help predict recovery. EEG analysis has the benefit of being able to be recorded at the patient's bedside, can be done for long periods of time in different states, and allows for study of cortical connectivity.

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