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Potential Utility of Resting-State Magnetoencephalography as a Biomarker of CNS Abnormality in HIV Disease

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Abstract

There is a lack of a neuroimaging biomarker for HIV-Associated Neurocognitive Disorder. We report magnetoencephalography (MEG) data from patients with HIV disease and risk-group appropriate controls that were collected to determine the MEG frequency profile during the resting state, and the stability of the profile over 24 weeks. 17 individuals (10 HIV+, 7 HIV−) completed detailed neurobehavioral evaluations and 10 minutes of resting-state MEG acquisition with a 306-channel whole-head system. The entire evaluation and MEG measurement were repeated 24 weeks later. Relative MEG power in the delta (0–4 Hz), theta (4–7 Hz), alpha (8–12 Hz), beta (12–30 Hz) and low gamma (30–50 Hz) bands was computed for 8 predefined sensor groups. The median stability of resting-state relative power over 24 weeks of follow-up was 0.80 with eyes closed, and 0.72 with eyes open. The relative gamma power in the right occipital ($t(15) = 1.99$, $p < .06$, $r = -.46$) and right frontal ($t(15) = 2.15$, $p < .05$, $r = -.48$) regions was associated with serostatus. The effect of age on delta power was greater in the seropositive subjects ($r^2 = .51$) than in the seronegative subjects ($r^2 = .11$). Individuals with high theta-to-gamma ratios tended to have lower cognitive test performance, regardless of serostatus. The stability of the wide-band MEG frequency profiles over 24 weeks supports the utility of MEG as a biomarker. The links between the MEG profile, serostatus, and cognition suggest further research on its potential in HAND is needed.

Keywords

HIV; HIV-Associated Neurocognitive Disorder; Magnetoencephalography (MEG); Magnetic Source Imaging (MSI); Cognition; Reliability; Biomarker

1.0 Introduction

HIV-Associated Neurocognitive Disorder (HAND) is a group of clinical syndromes of increasing severity: asymptomatic neurocognitive impairment (ANI), HIV-associated mild neurocognitive disorder (MNCD), and HIV-associated dementia (HAD) (Antinori et al., 2007). ANI includes those individuals with mild deficits in performance on neuropsychological tests, but who have no observed abnormalities in everyday functioning. By contrast, MNCD requires that there are impaired activities of daily living, as well as an acquired mild-to-moderate impairment in cognitive function in at least two different cognitive domains (attention-information processing, language, abstraction-executive, complex perceptual motor skills, memory, including learning and recall, simple motor skills or sensory perceptual abilities). The diagnosis of HAD requires an acquired moderate-to-severe cognitive impairment, with marked difficulty in ADLs.

HAND affects the management, survival, and quality of life of affected patients and their families (Bridge, 1988). HIV-infected individuals have slowed mentation, increased choice reaction times, and memory loss that is more characteristic of a retrieval defect than an encoding or storage loss (Becker et al., 1995a; Becker et al., 1995b; Martin, 1994; Martin et al., 1993; Martin et al., 1992). Following the introduction of highly active anti-retroviral therapy (HAART), the patterns of neuropsychological deficits now include more signs of cortical involvement (Cysique et al., 2004; Sacktor et al., 2007), severe immunosuppression is no longer a requirement for HAD (Dore et al., 1999), and the nature of the links between virological markers, immunological markers and HAD are changing (Brew, 2004; McArthur et al., 2003). Cognitive dysfunction persists even with the use of HAART (Sacktor et al., 2002) and undetectable CSF HIV does not necessarily prevent the progression of disease. HAD tends to develop when CD4+ T-lymphocyte cell counts fall below 200 cells/mm³ (Childs et al., 1999; Dore et al., 1999) as low CD4+ cell counts may indicate active HIV replication, enhancing the risk of hematogenous seeding and damage to the brain over time.

One major weakness in the clinical management and research efforts regarding HAND is the lack of a useful biomarker that reflects the underlying disease pathology (Antinori et al., 2005). Indeed, “[the] *current approaches to classification and diagnosis [of HAND] rely on syndromic definitions or measures of abnormality on neuropsychological testing in the background context of HIV-1 infection.... Supplanting or augmenting these approaches with objective biologic measurements related to underlying disease processes would provide a major advance in classification, diagnosis, epidemiology, and treatment assessment*” (Price et al., 2007)}, pg. 1781f).

In the search for such a biomarker, MRI-based measurement of cerebral blood flow (Alsop and Casement, 2004; Ances et al., 2009), functional MRI (fMRI) (Ernst et al., 2002; Juengst et al., 2007) and MR spectroscopy (e.g., (Chang et al., 2004; Paul et al., 2007)) have been tried, but have limitations. In addition to the limits placed on utilization based on patient characteristics (e.g., metal implants, claustrophobia, etc.), MR measures are generally indirect, relying on, for example, a hemodynamic response rather than measuring neuronal function directly. One technology that *can* measure brain function directly, and that has not been tested in HAND is magnetoencephalography (MEG).

MEG records neuronal activity from the magnetic fields induced by synchronized intraneuronal currents (George et al., 1995; Manoach et al., 2001) in large neuronal assemblies of at least $\sim 10^4$ – 10^5 pyramidal cells. This provides “a more direct index of sensory, motor, and cognitive task-specific activation compared with methods that rely on hemodynamic measures” (Papanicolaou et al., 2004), page 869). MEG has to balance the weakness of the signal ($\sim 10^3$ femtoteslas) against the strength of the noise ($\sim 10^9$ femtoteslas) by using hundreds of superconducting quantum interference devices (SQUIDs) incorporated in the whole head system and used in a magnetically shielded room (MSR) (Manoach et al., 2001). Like other electrophysiological measures (e.g., qEEG), MEG provides nearly simultaneous recording with respect to the neuronal events, meaning that subtle differences (esp., those related to cognitive “slowing”) are more likely to be detected, providing the opportunity for a more fine-grained analysis of functional connectivity (Stam et al., 2006). However, unlike these other methods, the poorly conducting skull bone that interferes with electrical, but not magnetic field patterns do not affect MEG. This means that MEG can localize and separate the contributions of multiple simultaneously active sources better than EEG, which translates into access to functional brain networks, which is more difficult with EEG than with MEG.

Because of the great sensitivity of MEG, and the various factors that can cause artifacts in the data, there are critical prerequisite data that need to be gathered, including determining the stability of the relevant features of MEG data over time. In order for MEG to be useful in tracking the natural history of CNS function in HIV disease (or any neurological disorder), or to be used in evaluating pharmacotherapy, we must first understand the extent to which the data are reproducible over time, and whether there are differences in the biomagnetic signature that are linked to serostatus or to cognition. The purpose of this pilot study was to obtain MEG data from a group of patients with HIV disease and risk-group appropriate controls to determine the reproducibility of MEG data over 24 weeks, and the effects of serostatus on these data.

2.0 Methods

2.1 Standard Protocol Approvals, Registrations, and Patient Consents

The Institutional Review Board at the University of Pittsburgh approved this study. Written informed consent was obtained from all participants prior to their undergoing research procedures.

2.2 Subjects

10 HIV-infected and 7 risk-group appropriate seronegative controls participated in this research. The subjects were 40–65 (mean: 51.5) years old, and all but one were men. The risks for HIV infection for both the infected and uninfected participants included having unprotected sex with men (among the men only) and using illicit injection drugs. All of the subjects were right-handed (Oldfield, 1971), native English speakers, without histories of ADD/ADHD or other developmental disabilities (by self report). The subjects did not have active drug/alcohol abuse or dependence, current major depression, or history of a neurological disease, CNS opportunistic infections, CNS tumors, or stroke. All of the HIV-infected participants were taking combination antiretroviral therapy; duration of infection was not available on all of the participants, but it was estimated at greater than 10 years, on average.

2.3 Procedures

2.3.1 Neuropsychological Studies—A detailed neuropsychological examination was completed at study entry and after 24 weeks. The evaluation comprised measures of multiple

cognitive domains including memory, language, visual construction, psychomotor speed, motor and executive functions; it was sensitive to the cognitive impairments associated with HIV disease (Becker et al., 2004), and provided the necessary information to complete the diagnostic adjudication using the Consensus Diagnostic criteria (Antinori et al., 2007). The test scores were converted into standardized values (i.e., T-scores) and then a summary variable was created for each cognitive domain, as well as a summary of Global Impairment using standard procedures (Woods et al., 2004). These standardized scores ranged from Normal [(1–3)], through Borderline [(4)], to five levels of impaired performance [(5–9)]. For the purpose of this study, we classified each subject as either Normal/Borderline [(1–4)] or Impaired [(5–9)].

2.3.2 Psychosocial Evaluation—Each participant underwent a semi-structured diagnostic interview, and completed questionnaires concerning psychiatric symptomatology. The components of the evaluation were: i) a modified Structured Clinical Interview for DSM-III-R (SCID) (Spitzer et al., 1990); ii) the Brief Symptom Inventory (Derogatis and Spencer, 1982) and the Neuropsychiatric Inventory (Cummings et al., 1994) to assess subclinical psychiatric symptoms, and iii) Heaton's Patient's Assessment of Own Functioning questionnaire (Heaton and Pendelton, 1981) and the Modified IADL scale (Lawton and Brody, 1969) to provide information about the specific symptoms of cognitive decline, and their impact on activities of daily living.

2.3.3 Structural MRI Scan—Each subject had an MRI exam of the brain for use with the MEG data. The scans were completed on a Siemens 3T TIM Trio using a protocol that was modified from that of the Alzheimer's Disease Neuroimaging Initiative (Mueller et al., 2005). The sagittal Magnetization Prepared Rapid Acquisition Gradient Echo (MP-RAGE) sequence was used with a FOV = 256 mm; slices = 160; TR = 2300 ms; TE = 2.91 ms; TI = 900 ms; Flip angle = 9 degrees; slice thickness = 1.2 mm.

2.3.4 MEG Data collection—The Elekta Neuromag® (Elekta Oy, Helsinki, Finland) MEG system has 102 magnetometers and 204 planar gradiometers in a helmet-shaped array covering the entire scalp. The magnetometers measure the overall magnitude of the magnetic field component approximately normal to the head surface; the gradiometers measure the difference of that field component at two adjacent locations. Eye movements were monitored by simultaneously recording an electro-oculogram. The MEG sensor unit, the floor-mounted gantry, the movable subject chair, together with the patient audio-visual monitoring and stimulus delivery systems, were all contained in a magnetically shielded room (Imedco AG, Hägendorf, Switzerland).

The participants were seated with their head in the MEG sensor helmet that covered the entire head except the face. Four head position indicator coils (HPI) were placed on the scalp, appropriately spaced in the region covered by the MEG helmet. The locations of three cardinal anatomical landmarks (nasion and two preauricular points), and the four HPI coils were digitized prior to each MEG study using a 3D-digitizer (ISOTRAK; Polhemus, Inc., Colchester, VT) to define the subject-specific Cartesian head coordinate system. Additional 30–50 anatomical points were digitized on the head surface to provide for a more accurate co-registration of the MEG data with the reconstructed volumetric MR image.

Once a subject was comfortably positioned in the MEG machine, short electrical signals were sent to the HPI coils to localize them with respect to the MEG sensor array. MEG data were acquired at a sampling rate of 1 kHz, with on-line filtering of 0.10–330 Hz. Acquisition occurred in two runs in a single session separated by approximately 10 minutes. The first run included two memory tasks, while the second run included the same two

memory tasks, as well as 10 minutes of “resting state” data; 5 minutes with eyes open followed by 5 minutes with eyes closed. These resting state data are the topic of this report.

2.3.5 MEG Data Analysis—The temporal extension of the Signal Space Separation method (Taulu and Simola, 2006; Taulu et al., 2004) was used to remove interference caused by sources outside of the MEG helmet and to align the signals to a standard head position. The Signal Space Projection method (Uusitalo and Ilmoniemi, 1997) was then used to remove any remaining artifacts after visual inspection. The data were then low-pass filtered at 100 Hz and downsampled to 256 Hz.

The resting-state data were divided into consecutive 3-second epochs, and a frequency analysis was performed in each segment using tools from FieldTrip (Oostenveld et al., 2011). We used the default multitaper method with discrete prolate spheroidal sequences (Slepian sequences) as tapers. The power estimates of the different frequencies were then averaged across the segments. Finally, the power in each channel was integrated over pre-defined bands (delta = 0–4 Hz, theta = 4–7 Hz, alpha = 8–12 Hz, beta = 12–30 Hz, gamma = 30–50 Hz), and the power in each band was summed over the magnetometer channels covering the specific regions of interest.

The analysis of the MEG data was done in sensor space, and in order to reduce the potential for interference in the data (e.g., muscle artifact), we did not include sensors at the boundaries/rim of the helmet. We also assigned sensors to regions (i.e., frontal, temporal, parietal, occipital) so that there was a “gap” between the different regions as a way to minimize any cross-talk (Supplemental Figure E-1 shows the specific sensors used in the analyses).

We converted the raw power values into percentages of the total of the region being analyzed. For example, we calculated the whole-brain relative power in the delta frequency band by first summing the whole brain power in each of the five frequency bands, then dividing the delta power by the total, and multiplying the result by 100 (i.e., (regional delta/whole-brain delta)*100). This operation was repeated for each frequency band at the level of the individual regions (i.e., frontal, parietal, temporal and occipital), separately for each hemisphere.

The ratio between the theta and gamma frequency band power has been found to be associated with cognitive impairment and with mesial temporal lobe atrophy (Moretti et al., 2009). Therefore, we also calculated the theta-to-gamma power ratio for each of the four brain regions by dividing the raw power in the theta band by the raw power in the gamma band. Thus, with the exception of the theta-to-gamma ratios, all of the analyses reported below utilize relative power data.

Several different parametric statistical tools were applied to the MEG data. The stability of the measures over time was assessed using the intra-class correlation (ICC). Independent sample *t*-tests, analyses of variance and linear regression models were used to compare MEG data using several different independent variables. Measures of effect size were correlation coefficients (*t*-tests), η^2 (ANOVA), and the standardized regression coefficient (β).

Raw MEG power values, broken down by study group, region, frequency band and time are presented in Supplemental Data Table E-1. In addition, “empty-room” data were acquired in conjunction of all follow-up recordings, and the analyses described above were all repeated on the empty-room data. None of those tests were statistically significant which implies that the effects reported below are not due to background noise.

3.0 Results

Because of the limited scope of the project, both in terms of the dependent variables of interest and the number of study participants, we are necessarily limited in statistical power. Consequently, we focus our attention more on measures of effect size than on traditional cut-off scores of statistical significance.

3.1 Stability

The stability of the individual frequency bands, by region, by hemisphere, and by condition (eyes closed vs. eyes open) is shown in Table 2. The power measured in these regions during the eyes-closed condition had a median stability (ICC) of $r = .82$ (range: 0.35–0.94). The highest stability was in the temporal lobes, and the lowest in the frontal lobes. In the eyes-open condition, stability was somewhat lower, with a median of $r = .72$ (range: 0.03–0.89). The highest stability was again found in the temporal lobe, with the lowest in the frontal region. Overall, the gamma frequency band showed the lowest stability across all regions and in both eyes open and eyes closed conditions.

3.2 Effects of HIV Serostatus

The resting-state whole-brain power data measured at the baseline visit were analyzed using independent sample t-tests (See Table 3). There were no significant effects of serostatus or visit on relative power on a region-by-region basis. However, there was an effect of serostatus on the whole-brain gamma power ($t(15) = 1.97, p < .06, r = -.45$), so we followed these analyses with comparisons of each of the regional gamma frequency data. The right occipital ($t(15) = 1.94, p < .06, r = -.45$) and right frontal ($t(15) = 2.15, p < .05, r = -.48$) regions also showed effects of serostatus (See Table 3).

3.3 Effects of other Variables of Interest

Analyses of whole-brain power (by frequency bands) during the eyes-open condition at the baseline visit revealed that power in the gamma ($t(15) = 2.04, p = .06, r = .47$) and theta ($t(15) = -2.52, p = .024, r = .55$) bands was related to the presence of cognitive impairment (present/absent). Power in the delta frequency was affected by age, but primarily among the HIV-infected subjects. When delta power was regressed on age and serostatus, age ($\beta = -.53, t(14) = -2.31, p = .04$) was significantly associated with delta power, while serostatus was not ($\beta = -.17$). There was an interaction between age and serostatus ($\beta = -.56, t(14) = -2.05, p = .06$); the association between age and delta power was small ($r^2 = .11$) in the seronegative subjects, but large ($r^2 = .51$) in the HIV+ subjects (Figure 1).

Finally, we examined the predictors of high theta-to-gamma ratios measured at the baseline visit (Moretti et al., 2009). We found that while serostatus was unrelated to any of the measures (all r 's $< .32$, all p 's $> .20$), cognitive impairment was important. Specifically, the subjects with impaired test performance – both HIV infected and uninfected - had higher theta-to-gamma ratios than those participants with Normal/Borderline performance in the temporal ($t(15) = 2.26, p = .04, r = .50$), parietal ($t(15) = 2.71, p = .02, r = .57$), and occipital regions ($t(15) = 2.18, p = .05, r = .49$), while the frontal region did not show a significant effect ($t(15) = -1.06, p = .31, r = .26$) (See Figure 2).

4.0 Discussion

These data make several points relevant to the consideration of the relative merits of MEG as a biomarker of the effects of HIV disease on the brain. First, at least in terms of relative power, and within the constraints of a small pilot study, the stability of the MEG data over six months is good. Second, it appears that differences in the gamma frequency band may

discriminate between the control subjects and those with HIV disease. Third, we replicated previous findings that theta:gamma ratios were linked to performance on neurological tests.

This study was designed to evaluate the reproducibility of MEG measurements over time. In this context, we use the term stability to refer to test–retest reliability that persists over a longer time period: in our case 24 weeks. This concept differs from the reliability that is measured over the short term, e.g., over two consecutive runs in a single measurement sessions, which is not affected by fluctuations in the physiological state that may occur over a longer period of time. The study sample is small due to cost constraints, but the size of the correlations between measures taken six months apart are such that they show that MEG may be useful in HIV clinical research settings, as well as with other neurological disorders. Further, although some of the statistical tests do not meet the standard threshold of $\alpha = .05$, the effect sizes are large, often accounting for more than 25% of the variance in a particular comparison.

Using a relatively simple measure of brain activity, relative power, we were able to obtain excellent reproducibility over the six-month follow-up period. This is important because to the extent that these, or similar measures are found in larger studies to reliably distinguish individuals with HIV disease or HAND from unaffected controls, they must be shown to remain relatively unchanged over time unless there is an intervening event (e.g., pharmacotherapy or physiological change secondary to disease progression). This stability is a prerequisite for a useful biomarker in studies of the natural and treated history of HIV disease. However, our data give some promise to the idea that MEG may be useful in clinical trials and for tracking disease progression. Also, to the extent that MEG data can detect a difference in CNS function between groups, this means that it may be possible to identify individuals with HIV-related brain disease, in the absence of a *clinical* syndrome (i.e., presymptomatic diagnosis). In that regard, it would be interesting to determine the extent of the change in the MEG frequency profile when infected patients are first exposed to HAART.

Gamma band activity is important for cognitive processing (see, e.g., reviews by Herrmann and colleagues (Herrmann and Demiralp, 2005; Herrmann et al., 2010)). Of particular importance may be the fact that gamma band responses are highly correlated with response latencies—slowing of behavioral responses are associated with increasing amplitudes of gamma. Gamma responses are generally considered to play an important role in perceptual binding. It has been shown that higher gamma level during memory encoding of a stimulus predicts the success of subsequent recall, and there is higher gamma during the encoding of words that are recognized at a later time (compared to those not recognized). Further, activity in the lower end of the gamma band, as we measured here, may reflect synchronization between cortical areas (Kaiser and Lutzenberger, 2005), which suggests that there may be merit in examining functional connectivity in HIV-infected individuals.

The finding that there are between-group differences in the gamma frequency band differs from that found among older individuals with Mild Cognitive Impairment or Alzheimer's Disease (Fernandez et al., 2006a; Fernandez et al., 2006b; Maestu et al., 2008; Maestu et al., 2006), where abnormalities occur primarily in the delta band. While we found that delta power was correlated with age, it was not associated with cognitive impairment in this younger age group. However, the significant interaction between age and serostatus is consistent with neuropsychological data that find that the effects of age on cognitive functions can be greater in HIV-infected individuals (see, e.g., (Becker et al., 2004)). While it may be tempting to interpret these findings in light of a “premature aging” hypothesis, the size of our sample means that we cannot distinguish between age, duration of infection, and the impact of other comorbidities on the MEG frequency profile. However, our data do

suggest that further investigation with a larger sample, with a wider age range could reveal important aspects of NeuroAIDS not appreciated with other neuroimaging modalities.

Finally, our data are more generally relevant to the utility of MEG in other neurological conditions. Much of the clinically relevant MEG research uses activation protocols that focus either on somatosensory functions (e.g., (Lee et al., 2006)) or, more prominently, language tasks in the context of presurgical functional localization studies (Missonnier et al., 2006). MEG is generally reliable and valid (relative to sodium amytal studies) (Liljestrom et al., 2005), and more recent data have confirmed the reproducibility of the MEG signal. The source of MEG signal localization varies within a range of 1.5 – 3 mm (Liljestrom et al., 2005). MEG signal reliability for a single region was $\rho=.42$, and the median correlation across more than 20 regions was .61 (with only one region having a correlation less than .50) (Yoo et al., 2005). Thus, for language-based tasks, the ability to localize MEG signal appears good (Missonnier et al., 2006). Our data add to this corpus of work by demonstrating that resting state data has good reproducibility over 24 weeks, and thus may be a useful tool to add to the armamentarium of clinical trials and longitudinal studies of brain function and disease.

This is a small-scale, cross-sectional, observational study with all of the attendant limitations. Because the sample was small, we relied more on effect sizes than on alpha levels. With a larger sample size, we would be able to complete a Receiver Operating Characteristic analysis to provide appropriate quantitative support to our data that suggest that MEG power may be able to discriminate HIV-infected individuals from uninfected controls. All of our HIV+ participants were healthy, with all but one showing little or no detectable viral replication; CD4+ cell counts were generally normal (i.e., >500). They had all been infected (and treated) for more than 10 years, so we could not evaluate the impact of early therapy on the MEG data. There was only one woman in the sample, although her data did not differ from that of the men, meaning that we could evaluate sex differences (or differences in mode of HIV transmission). In addition, because these analyses were conducted in sensor space, we did not take advantage of the spatial resolution of MEG. Clearly, future studies will need to include analyses in source (i.e., brain) space, in order to directly compare/contrast functional and structural changes secondary to HIV disease. These are all important questions that need to be addressed in future studies, but they are beyond the restricted aims of the current project.

4.1 Conclusions

We cautiously conclude that the MEG has the potential to be a useful biomarker; wide-band power data were stable over 24 weeks and possibly differentially sensitive to serostatus and to cognitive impairment. Larger trials of subjects evaluated with MEG will confirm the utility of this novel physiological measure.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Scatterplot of the relative power in the Delta band (0–4 Hz) (vertical axis) as a function of age (horizontal axis). HIV-infected individuals are shown with the filled circles (solid line) and the uninfected subjects with the open circles (dashed line).

Figure 2. Mean of the Theta: Gamma ratios (vertical axis) as a function of the sensor locations and presence of cognitive impairment (open bars are Normal/Borderline) in all study subjects.

Table 1

Characteristics of Study Participants as a Function of Serostatus Mean (S.D.)

	Seronegative	Seropositive	Statistics ¹
Number	7	10	
Age	53.0 (6.5)	50.5 (4.8)	.96, .23
Education	14.1 (1.7)	14.4 (2.0)	-.34, .08
Grade Level Reading	12.4 (1.3)	11.6 (2.3)	.85, .20
CD4+ Cell Count	n/a	776.0 (268)	n/a
Viral Load (log₁₀)	n/a	2.77 (3.11)	n/a
Cognitive Functions			
Executive	1.56 (1.0)	2.90 (1.4)	-2.4, .50 ²
Fluency	2.22 (1.3)	2.80 (1.5)	-.90, .21
Attention	1.56 (.53)	1.80 (.63)	-.91, .22
Speed	1.89 (1.1)	2.90 (2.2)	-1.2, .29
Learning	3.67 (3.6)	3.40 (2.7)	.18, .04
Memory	3.67 (3.5)	4.10 (2.6)	-.31, .08
Motor	1.22 (.44)	2.10 (2.1)	-1.2, .28
Spatial	1.33 (.71)	2.20 (1.8)	-1.3, .31
Global	4.00 (3.4)	4.20 (2.3)	-.15, .04
Global Impairment (%(N))	43 (3)	60 (6)	.49, .17

¹) t and r (as effect size), χ^2 and Φ ²) $p < .05$

Table 2

a: 24-Week Stability of Measures of Relative Power (Eyes Closed)					
	Delta	Theta	Alpha	Beta	Gamma
Frontal					
Left	.815	.866	.804	.837	.518
Right	.857	.938	.881	.860	.543
Temporal					
Left	.843	.941	.848	.880	.698
Right	.874	.901	.772	.885	.669
Parietal					
Left	.803	.822	.772	.820	.516
Right	.807	.853	.733	.862	.352
Occipital					
Left	.752	.906	.753	.849	.537
Right	.770	.910	.758	.838	.483

b: 24-Week Stability of Measures of Relative Power (Eyes Open)					
	Delta	Theta	Alpha	Beta	Gamma
Frontal					
Left	.324	.060	.196	.364	.339
Right	.336	.045	-.028	.250	.338
Temporal					
Left	.836	.818	.887	.814	.428
Right	.679	.842	.718	.792	.241
Parietal					
Left	.695	.818	.806	.817	.272
Right	.668	.807	.729	.831	.028
Occipital					
Left	.784	.797	.851	.780	.216
Right	.835	.823	.855	.838	.261

Table 3

A: Relative Power by Region, Band, Time and Serostatus Eyes Open				
	HIV Negative Controls		HIV Infected	
	Baseline	Follow-up	Baseline	Follow-Up
Whole Brain				
Delta	35.8 (2.7)	36.4 (3.6)	33.9 (2.8)	36.3 (2.8)
Theta	16.3 (1.1)	16.4 (1.0)	17.3 (.90)	17.4 (.80)
Alpha	12.5 (2.2)	13.0 (2.0)	14.9 (1.7)	14.5 (1.5)
Beta	29.3 (3.1)	29.2 (3.2)	29.5 (2.4)	27.5 (2.5)
Gamma	6.16 (.73) *	5.01 (.71)	4.46 (.56)	4.32 (.56)
Frontal				
Delta	18.5 (2.9)	18.2 (2.2)	18.2 (2.3)	17.1 (1.7)
Theta	47.3 (7.6)	32.5 (24)	45.7 (11)	49.4 (8.5)
Alpha	17.4 (1.3)	11.9 (9.3)	17.6 (2.0)	17.7 (2.7)
Beta	7.96 (1.3)	5.78 (5.1)	9.35 (4.7)	8.49 (1.5)
Gamma	21.4 (6.0)	11.7 (7.7)	22.7 (7.2)	19.3 (5.8)
Temporal				
Delta	5.94 (1.9)	2.69 (1.3)	4.67 (1.6)	5.11 (1.6)
Theta	33.6 (3.0)	32.0 (3.1)	34.8 (2.3)	33.9 (2.4)
Alpha	36.2 (6.4)	36.2 (9.4)	34.2 (10)	31.9 (9.8)
Beta	17.4 (1.2)	17.9 (2.6)	17.7 (3.3)	17.9 (3.6)
Gamma	13.7 (2.4)	15.0 (4.4)	15.3 (6.5)	17.1 (6.8)
Parietal				
Delta	28.0 (5.6)	26.7 (8.2)	28.7 (8.3)	29.2 (8.0)
Theta	4.60 (.41)	4.09 (2.1)	4.11 (1.5)	3.92 (2.0)
Alpha	22.0 (2.5)	23.9 (3.6)	22.4 (1.9)	21.8 (2.8)
Beta	30.8 (4.6)	33.3 (6.8)	28.8 (9.0)	30.5 (11)
Gamma	14.8 (1.7)	16.4 (2.6)	15.3 (4.0)	15.7 (3.6)
Occipital				
Delta	12.6 (2.2)	13.8 (3.5)	14.4 (5.5)	14.6 (5.6)
Theta	35.1 (5.3)	30.7 (7.2)	35.7 (11)	33.7 (12)
Alpha	6.67 (1.4)	5.75 (2.8)	5.76 (1.8)	5.43 (1.9)
Beta	25.9 (2.9)	25.8 (2.6)	24.6 (2.2)	27.2 (2.0)

A: Relative Power by Region, Band, Time and Serostatus Eyes Open				
	HIV Negative Controls		HIV Infected	
	Baseline	Follow-up	Baseline	Follow-Up
Delta	33.4 (6.2)	31.8 (12)	30.7 (11)	28.4 (13)
Theta	17.1 (1.5)	19.0 (3.8)	18.1 (3.7)	18.9 (4.1)
Alpha	14.9 (2.3)	18.5 (5.6)	17.8 (6.9)	21.3 (8.0)
Beta	29.7 (6.2)	27.0 (11)	29.2 (8.7)	28.4 (9.4)
Gamma	4.83 (.88)	3.69 (1.8)	4.20 (1.5)	3.06 (1.6)

B: Relative Power by Region, Band, Time and Serostatus Eyes Closed				
	HIV Negative Controls		HIV Infected	
	Baseline	Follow-up	Baseline	Follow-Up
Whole Brain				
Delta	34.2 (4.1)	36.3 (4.2)	28.6 (3.2)	31.5 (3.3)
Theta	18.1 (1.2)	17.8 (1.4)	18.3 (1.0)	17.7 (1.0)
Alpha	16.2 (2.6)	14.8 (2.5)	19.6 (2.0)	17.2 (1.9)
Beta	27.5 (3.2)	26.7 (3.5)	29.5 (2.5)	29.5 (2.7)
Gamma	3.93 (.63)	4.34 (.84)	3.97 (.50)	4.09 (.65)
Frontal	16.0 (2.2)	17.7 (2.2)	14.3 (1.7)	13.9 (1.7)
Delta	48.5 (8.5)	50.9 (6.4)	42.4 (8.6)	19.2 (8.5)
Theta	18.1 (2.0)	18.2 (1.7)	17.5 (2.3)	7.50 (2.7)
Alpha	9.00 (2.5)	8.65 (2.3)	11.0 (4.1)	4.22 (1.5)
Beta	19.8 (7.1)	18.3 (5.9)	23.9 (6.8)	10.7 (5.8)
Gamma	4.60 (1.7)	4.00 (1.9)	5.13 (1.6)	2.28 (1.7)
Temporal	32.8 (2.7)	32.1 (3.2)	33.8 (2.1)	34.5 (2.4)
Delta	35.4 (8.0)	36.2 (9.4)	29.8 (10)	31.9 (10)
Theta	18.4 (2.9)	17.9 (2.6)	18.6 (3.0)	17.9 (3.6)
Alpha	15.8 (4.0)	15.0 (4.4)	19.3 (7.0)	17.1 (6.8)
Beta	26.8 (8.4)	26.7 (8.2)	28.5 (6.7)	29.2 (8.0)
Gamma	3.57 (1.2)	4.09 (2.1)	3.74 (1.7)	3.92 (2.0)
Parietal	21.4 (2.6)	20.5 (2.9)	20.6 (2.0)	20.4 (2.3)

B: Relative Power by Region, Band, Time and Serostatus Eyes Closed				
	HIV Negative Controls		HIV Infected	
	Baseline	Follow-up	Baseline	Follow-Up
Delta	31.2 (6.1)	33.3 (6.8)	27.4 (8.9)	30.5 (11)
Theta	16.7 (3.1)	16.4 (2.6)	16.3 (2.6)	15.7 (3.6)
Alpha	15.1 (3.0)	13.8 (3.5)	17.1 (6.0)	14.6 (5.6)
Beta	31.7 (8.2)	30.7 (7.2)	33.7 (7.3)	33.7 (12)
Gamma	5.27 (2.0)	5.75 (2.8)	5.55 (2.0)	5.43 (1.9)
Occipital	29.8 (2.5)	29.8 (2.4)	31.4 (2.0)	31.2 (1.9)
Delta	29.0 (11)	31.8 (12)	23.7 (13)	28.4 (13)
Theta	19.3 (3.9)	19.0 (3.8)	19.5 (3.4)	18.9 (4.1)
Alpha	20.2 (6.0)	18.5 (5.6)	24.2 (8.7)	21.3 (8.0)
Beta	28.2 (11)	27.0 (11)	29.6 (7.8)	28.4 (9.4)
Gamma	3.31 (.96)	3.69 (1.8)	3.01 (1.6)	3.06 (1.6)

* p<.05