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Alpha Rhythm And The Default Mode Network: An Eeg/Fmri Study

Anthony Dean Bowman
University of Alabama at Birmingham

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by

ANTHONY D. BOWMAN

JERZY P. SZAFLARSKI, CHAIR
ALLAN C. DOBBINS
TIMOTHY J. GAWNE
KRISTINA M. VISSCHER

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ANTHONY DEAN BOWMAN

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ABSTRACT

Reports of the relationship between the default mode network (DMN) and alpha power are conflicting in the literature. Our goal for this study was to assess this relationship by analyzing concurrently obtained EEG/fMRI data using hypothesis-independent methods. To accomplish this, we collected fMRI and EEG data during eyes-closed rest in 20 participants aged 19-37 (10 females) and performed independent component analysis on the fMRI data and a Hamming windowed Fast Fourier Transform on the EEG data. We correlated fMRI fluctuations in the DMN with alpha power. Of the six independent components (ICs) found to have significant relationships with alpha, four contained DMN-associated regions: one IC was positively correlated with alpha power while all others were negatively correlated. Furthermore, two ICs with opposite relationships with alpha had overlapping voxels in the medial prefrontal cortex (MPFC) and posterior cingulate cortex (PCC) suggesting that subpopulations of neurons within these classic nodes within the DMN may have different relationships to alpha power. Different parts of the DMN exhibit divergent relationships to alpha power. Our results highlight the relationship between DMN activity and alpha power, indicating that networks, such as the DMN, may have subcomponents that exhibit different behaviors.

Keywords: EEG/fMRI, default mode network, alpha power, independent component analysis, thalamus

DEDICATION

For my family.

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INTRODUCTION

A brain at rest still exhibits activity with reliable patterns, observable through a variety of techniques (Arieli et al., 1996, Kay et al., 2012, Knyazev et al., 2011). Using functional magnetic resonance imaging (fMRI), "resting state" networks can be defined as synchronous fluctuations in the blood oxygenation level dependent (BOLD) signal between brain regions (Damoiseaux et al., 2006, Morgan et al., 2008). While at rest, the activity in one such network, the default mode network (DMN), is known to increase, decreasing while a subject performs a task (Mantini et al., 2007, Shulman et al., 1997a, Shulman et al., 1997b). The DMN typically includes regions of the medial prefrontal cortex (MPFC), anterior and posterior cingulate cortex (PCC), cuneus/precuneus, and temporo-parietal junction/angular gyrus (Buckner et al., 2008, Greicius et al., 2009, Mantini et al., 2013) with increased activations within the network linked to introspection ("internal mentation") and integration of thought processes (Kay et al., 2012, Mason et al., 2007).

During the resting state, scalp electroencephalography (EEG) can also be used to observe the oscillations of neural activity in the brain (Berger, 1929). At rest, activity in the 8 to 13 Hz range generally recorded from posterior/occipital electrodes, known as the alpha rhythm, has been shown to increase, especially when a subject's eyes are closed (Berger, 1929). Because alpha power has been shown to decrease while a subject is attending to visual stimuli (Knyazev et al., 2011, Petsche et al., 1997) it is thought alpha

power is a measure of a subject's selective attention to visual objects (Foxe and Snyder, 2011; Payne and Sekuler, 2014).

With activity in the DMN and alpha power both shown to increase during the resting state, previous studies have attempted to reveal the relationship between them with mixed results. In recent years, development of preprocessing tools to remove gradient and electrocardiogram artifacts from EEG data has allowed for a method combining fMRI with continuous EEG data recorded simultaneously (Allen et al., 2000, Stern, 2006). While this method does to a degree compensate for the poor spatial resolution of the EEG by coupling it with the high spatial resolution of fMRI (Koles, 1998, Pascual-Marqui, 1999), studies employing this method have still produced varied results (Difrancesco et al., 2008, Goldman et al., 2002, Laufs et al., 2003a, Laufs et al., 2003b). With these previous studies employing hypothesis driven analyses, others have applied hypothesis-independent (data-driven) methods. Independent component analysis (ICA) is one such method which can identify spatially distributed brain regions that act in concert. Previous studies which employed ICA have still showed different results in which regions showed positive, negative, or no significant correlation to alpha power (Mantini et al., 2007, Neuner et al., 2013). To shed further light on the relationship between alpha and the DMN, we gathered simultaneous fMRI and EEG data. Regions of the DMN were identified by ICA and cross-correlated with alpha frequency power extracted from the EEG data using a Hamming windowed fast Fourier transform method similar to one previously published (Difrancesco et al., 2008).

RELATIONSHIP BETWEEN ALPHA RHYTHM AND THE DEFAULT MODE NETWORK: AN EEG-FMRI STUDY

by

ANTHONY D. BOWMAN, JOSEPH C. GRIFFIS, KRISTINA M. VISSCHER, ALLAN C. DOBBINS, TIMOTHY J. GAWNE, MARK DIFRANCESCO, JERZY P. SZAFLARSKI

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Abstract

Introduction:

Reports of the relationship between the default mode network (DMN) and alpha power are conflicting. Our goal was to assess this relationship by analyzing concurrently obtained EEG/fMRI data using hypothesis-independent methods.

Methods:

We collected fMRI and EEG data during eyes-closed rest in 20 participants aged 19-37 (10 females) and performed independent component analysis on the fMRI data and a Hamming windowed Fast Fourier Transform on the EEG data. We correlated fMRI fluctuations in the DMN with alpha power.

Results:

Of the six independent components (ICs) found to have significant relationships with alpha, four contained DMN-associated regions: one IC was positively correlated with alpha power while all others were negatively correlated. Furthermore, two ICs with opposite relationships with alpha had overlapping voxels in the medial prefrontal cortex (MPFC) and posterior cingulate cortex (PCC) suggesting that subpopulations of neurons within these classic nodes within the DMN may have different relationships to alpha power.

Conclusion:

Different parts of the DMN exhibit divergent relationships to alpha power. Our results highlight the relationship between DMN activity and alpha power, indicating that networks, such as the DMN, may have subcomponents that exhibit different behaviors.

Key words: EEG/fMRI, default mode network, alpha power, independent component analysis, thalamus

Even when at rest, the brain is active and this activity follows reliable patterns that can be observed using functional imaging techniques, as well as neurophysiological methods (Arieli et al. , 1996, Kay et al. , 2012, Knyazev et al. , 2011). During fMRI, the blood oxygenation level dependent (BOLD) signal in the brain is recorded over time. Synchronization of the low-frequency fluctuations of this signal between regions allows for the so-called "resting state" networks to be defined (Damoiseaux et al. , 2006, Morgan et al. , 2008). The default mode network (DMN) is one such resting state network, typically defined to include regions of the medial prefrontal cortex (MPFC), anterior and posterior cingulate cortex (PCC), cuneus/precuneus, and temporo-parietal junction/angular gyrus (Buckner et al. , 2008, Greicius et al. , 2009, Mantini et al. , 2013). Hippocampi, parahippocampal gyri, and fronto-polar cortex are sometimes included in the DMN as regions that are “loosely integrated” with the DMN because of their presence in some studies (Huijbers et al. , 2011, Samann et al. , 2011). Activity in the typical DMN regions is known to increase during the resting state and decrease when a subject is performing a task (Mantini et al. , 2007, Shulman et al. , 1997a, Shulman et al. , 1997b,). Increased activations within this network are related to the processes of memorization and creating associations (Buckner et al. , 2008). Increased activation of the DMN is thus typically linked to introspection or "internal mentation" and integration of thought processes (Kay et al. , 2012, Mason et al. , 2007,). However, while the fMRI measures that produced these results provide relatively fine spatial resolution in the millimeter range, the BOLD signal remains an indirect and slow measure of neural activity.

In contrast to fMRI, scalp EEG is a high temporal resolution measure of neural activity in the brain with a relatively poor spatial resolution (Burle et al. , 2015). EEG can measure

oscillations of neural activity in the brain which have been well documented (Berger, 1929). One such waveform is the alpha rhythm: activity in the 8 to 13 Hz range, typically recorded from posterior/occipital electrodes. These alpha oscillations have been observed to strengthen during rest, particularly when a subject's eyes are closed (Berger, 1929) and are typically modulated by performing cognitive tasks, in particular, they are selectively suppressed during directed visual attention (Knyazev et al. , 2011, Petsche et al. , 1997). Current thinking suggests that alpha power indexes the degree of selective attention toward visual objects (Foxe and Snyder, 2011; Payne and Sekuler, 2014). EEG is a temporally precise measure of neural activity, as it measures changes in electric fields, allowing for exploring neuronal firing patterns with high temporal resolution. However, limited spatial resolution and lack of direct access to the deep brain structures means that localization of EEG sources may be difficult (Koles, 1998, Pascual-Marqui, 1999).

The poor spatial resolution of the EEG can, to a certain degree, be handled by combining it with the high spatial resolution of fMRI. This method of combining EEG with fMRI (EEG/fMRI) in recent years has proven useful for examining the physiologic and pathophysiologic states of the brain (Difrancesco et al. , 2008, Goldman et al. , 2002, Kobayashi et al. , 2006, Pittau et al. , 2012). Development of preprocessing tools to remove gradient and electrocardiogram artifacts from EEG data has allowed for continuous EEG data to be analyzed in conjunction with imaging data, further opening up research opportunities (Allen et al. , 2000, Stern, 2006).

Previous attempts to elucidate the relationship between DMN activity and alpha oscillations have produced mixed results. The discrepancies between studies are not necessarily contradictory as different methods and techniques may lead to different results and conclusions. Earlier studies have correlated EEG with the results of resting PET (Sadato et al. , 1998, Schreckenberger et al. , 2004) and EEG with resting fMRI (eyes open or eyes closed) at magnetic field strengths between 1.5 to 4 T (Difrancesco et al. , 2008, Goldman et al. , 2002, Laufs et al. , 2003a, Laufs et al. , 2003b). All of the above-mentioned studies conducted hypothesis driven analyses to conclude that some brain regions e.g., thalamus or occipital cortex exhibit positive or negative relationship with alpha power. We identified only a few studies that applied hypothesis-independent (data-driven) methods to analyze EEG/fMRI data in order to examine the contributions of alpha power to the BOLD signal changes in the DMN regions. Independent component analysis (ICA) is a data driven method that can identify spatially distributed brain regions that act in concert. ICA makes no assumptions regarding the stimulus or brain response and does not require specification of the hemodynamic response function (HRF), providing an advantage over analytical approaches that require precise knowledge of the HRF. ICA allows for identification of temporary connections as well as more stable connections and is thus particularly useful for analysis of resting state fMRI data (Bartels et al. , 2004, Karunanayaka et al. , 2010, Kay et al. , 2013). One such ICA study identified two main resting state networks that were positively associated with EEG power in the alpha band – one corresponding to the DMN (bilateral parietal lobule, posterior cingulate and precuneus, and bilateral prefrontal cortices) and one related to self-referential mental activity (anterior cingulate, cerebellum, and hypothalamus). Since this study tested correlations with multiple EEG frequencies, the authors showed that one

region may have relationships with more than one EEG frequency and that these relationships can be independent of one another (Mantini et al. , 2007). Another ICA study did not identify any significant correlations with alpha power (Neuner et al. , 2013). These studies demonstrate that significant questions remain concerning the relationship between the DMN and alpha power. By using ICA, a method without a priori assumptions, we aim to shed further light on the alpha-DMN relationship. To do so, fMRI and EEG data were obtained simultaneously, voxels of the DMN network were identified by ICA and cross-correlated with alpha frequency power extracted from the EEG. While we expected to identify several components corresponding to the DMN, we hypothesized that only some of them, especially thalami and occipital cortices would correlate with alpha power.

1. Methods

2.1. Subjects

Twenty healthy adult subjects (10 women and 10 men; aged 19-37) participated in this EEG/fMRI study after providing written informed consent. They were recruited from the general university population. Study criteria required all subjects to be between 19 and 65 years of age, have a normal developmental history with no neurological conditions, have completed at least a high school education and have no contraindications to fMRI at 3T. The study was approved by the Institutional Review Board (IRB) at the University of Alabama at Birmingham. Each subject first underwent 10 minutes of resting state EEG collected outside of the scanner room for later comparison with data collected inside the

scanner to confirm data quality. For each resting state period subjects were instructed to keep their eyes closed, relax, and let their minds wander. Each subject underwent a T1-weighted anatomical scan and a resting state T2*-weighted functional scan with simultaneous EEG recording (EEG/fMRI).

2.2. MRI Acquisition and Preprocessing

The fMRI was performed on a Siemens Magnetom Allegra 3 Tesla scanner. A T1-weighted structural image was collected (TR = 2300 ms; voxel size of 1.0 x 1.0 x 1.0 mm; TE = 2.17 ms; FOV = 25.6 x 25.6 x 19.2 cm, matrix = 256 x 256 x 192 pixels with sagittal orientation) along with a T2*-weighted functional scan (TR = 2 seconds; voxel size of 3.8 x 3.8 x 4.0 mm; TE = 30 ms; slice thickness = 4 mm; FOV = 24 x 24 cm, matrix = 60 x 60 with sagittal orientation; flip angle = 70°) lasting for 10 minutes. The first two measurements (whole brain volumes) were excluded to allow for the scanner to achieve magnetic equilibrium, resulting in 298 measurements per scan. Each functional scan was then preprocessed with in-house MATLAB scripts using Statistical Parametric Mapping software (SPM12b, http://www.fil.ion.ucl.ac.uk/spm/) including slice timing and motion correction, normalization to the Montreal Neurological Institute template, and spatial smoothing using a Gaussian kernel (6 mm FWHM).

2.3. EEG Acquisition and Preprocessing

EEG data were recorded across 64 channels at 2 kHz both prior to placing the subject inside the scanner as well as during the functional scan. Electrocardiographic (ECG) data

were also collected using two electrodes for later ballistocardiographic (BCG) artifact removal. These data were collected continuously using an MR-compatible system (MagLink by Neuroscan, Inc., Charlotte, NC, USA) with Curry 7 software. Timing of the start of every fMRI volume acquisition was recorded and inserted into the EEG data as events. Preprocessing using Curry 7 included band pass filtering between 1 and 35 Hz, constant baseline correction, removal of the echo-planar image (EPI) artifact using a 15 sample rolling average of the EPI gradient artifact aligned to the inserted events, and BCG artifact suppression using the first three components from principal component analysis centered to the BCG artifact on a per subject basis applied to the ECG channel.

2.4. Image Processing

Independent component analysis (ICA) of fMRI data results in segmentation of brain regions into maximally independent components, each consisting of a spatial map of activation and corresponding time course (Calhoun et al, 2001). To quantify the reliability of each independent component across multiple runs of ICA, the Infomax algorithm of ICASSO with a minimum cluster size of 50 was applied to the fMRI data (Himberg et al, 2004). Group level independent component analysis was performed using the Group ICA of fMRI Toolbox (GIFT; http://mialab.mrn.org/software/gift/index.html), first generating 22 group level independent components (ICs) followed by back generation of individual subject independent components. This IC generation was performed fifty times by ICASSO with the generated ICs then compared and grouped into maximally independent clusters. The

stability index of each cluster was quantified by comparing intercluster and intracluster similarity as defined by Himberg et al (2004) with only those components with a stability index greater than 0.90 retained. Group level ICs were then visually screened and those consisting of mostly artifact (activation outside of the brain, within ventricles, etc.) were excluded from further analyses. For optimal comparison with alpha power, we elected to decompose our own fMRI data as opposed to using networks defined based on a previously published database from a different group of participants.

2.5. EEG Processing and Correlation

A time course of alpha power, with sampling coincident with imaging acquisition, was extracted from the original EEG data from four bipolar channels (P3-O1, P4-O2, P7-O1, P8-O2) using a method similar to one previously described (DiFrancesco et al, 2008). Each sample represented the mean power in the alpha frequency band of 8 - 13 Hz across the 4 bipolar channels using a Hamming-windowed fast Fourier transform spanning the corresponding imaging TR period of 2 seconds. After extraction, the resulting time course was convolved with the canonical hemodynamic response function as defined by SPM in order to better synchronize the temporal phase shifts of this EEG data and the BOLD data. This final alpha time course for each subject was correlated with the time course of each IC. The raw correlation coefficients were transformed into Fisher Z-scores and a one sample t-test performed on the set of z-scores for each IC. Multiple comparison correction using the false discovery rate method was then applied to the p-values obtained from each t-test (Benjamini and Hochberg, 1995).

3. Results

EEG-fMRI data from seventeen subjects were analyzed. Three of the original 20 subjects were excluded: two had insufficient data due to premature removal from the scanner and one because of an incidental finding. Group level independent component analysis (GICA) produced 22 ICs, all with stability indices above 0.90. Six of these ICs were found to have significant correlations to alpha ($p < 0.05$; Table 1) and four contained brain regions previously associated with the DMN (Figure 2). An example of an Independent Component time course and alpha power signal from one participant is shown in Figure 1, demonstrating the correlation between this alpha power signal and the BOLD response from the independent component.

The other two independent components with significant correlations to alpha power included one component comprised mainly of voxels in the cerebellum (IC10) and brain stem while the vast majority of the voxels in the other component were within the right frontal and right temporal lobes (IC4, Figure 3).

The four components shown in Figure 2 are consistent with DMN networks obtained in other fMRI studies employing ICA (Allen et al. , 2011, Heine et al. , 2012). More specifically, the division of activation within parietal and posterior cingulate cortices and activation in the MPFC into separate independent components found in this study mirrors results shown in the study by Allen et al. (2011). The components identified include voxels in the typical midline structures (MPFC, PCC, and thalamus in IC5, IC8, IC11,

and IC22) as well as lateral structures (posterior temporal, inferior parietal cortex in IC5 and IC22).

Of the 22 components identified with ICA, 16 were found to be not significantly correlated with alpha. These components include a deep occipital component, a more superficial occipital component, a bilateral component with voxels comprising the majority of both temporal lobes, a component including bilateral parietal lobes, a component with bilateral temporal activations with a cluster in the MPFC, and a component with bilateral superior temporal activations. The other 10 components not listed were excluded from analysis after visual inspection showed activations either primarily in the ventricles, external to the brain, or consistent with movement artifact.

4. Discussion

Applying ICA to EEG/fMRI data allows for hypothesis-free identification of DMN components that correlate with alpha power and for identification of sources within the same DMN region that may have different behavior and possibly opposite relationships to alpha power (Figure 4). This provides a key insight when considered in the context of DMN sub-networks and how the DMN relates to other brain networks.

Among the DMN networks identified in our study, all statistically significant correlations with alpha power were negative, with the exception of IC11. In that component, which comprises voxels primarily in the PCC and MPFC, BOLD signal changes were positively correlated with alpha ($p = 0.0052$). These regions are thought to participate in internal adaptive processes of retrieval, representation, and direct manipulation of various

working memory processes including organization, planning and problem solving (Binder et al. , 1999). The positive correlation of these anterior DMN nodes (IC11) with alpha is also consistent with the "internal mentation" hypothesis or introspection theory of alpha power (Mason et al. , 2007). We observed a strong spatial overlap between IC5 and IC11, as shown in Figure 4, indicating that these two components, despite their different relationships to alpha power, involve overlapping tissues.

The default mode network is observed to be preferentially active during resting state and in the absence of performing a task (Raichle et al, 2001). During resting state, the DMN is theorized to play a role in introspection, mind wandering or day dreaming (the "introspection" hypothesis; Mason et al, 2007), but is also theorized to assist in maintaining a level of outward vigilance, monitoring the environment for any stimuli that may require more direct, focused attention (the “sentinel” hypothesis; Raichle et al, 2001)(Gilbert et al. , 2007). The diagram on the right side of Figure 5 illustrates a model where, during rest, the neural system toggles between ‘sentinel’ and ‘introspection’ states. The DMN is hypothesized to contribute to each of these states and to shifting between them.

Given that the literature has ascribed a dual function to the DMN, it is reasonable to look for duality in the behavior of DMN regions. One duality to consider is the relationship to alpha power. To reiterate, high alpha power is thought to relate to suppression of attention to the external environment, and to be actively modulated in order to suppress potentially distracting sensory information (Foxe and Snyder, 2011; Payne and Sekuler, 2014). Suppression of sensory information is essential for introspection, in order that

sensory information does not interfere with introspective information processing. Thus, components of the DMN associated with introspection are expected to be positively correlated to alpha power. Indeed, a set of DMN regions that are linked to introspection (the more ventromedial regions in IC11) were positively correlated to alpha power (Gusnard et al, 2001). Further, the posterior cingulate/precuneus, a prominent node of the DMN, has been suggested to function in part to suppress sensory information processing (Buckner et al. , 2008), and this region was also included in the component (IC11) that was positively correlated to alpha power.

Conversely, the proposed 'sentinel' function of the DMN requires maintaining a level of outward vigilance and taking in sensory information. Brain regions with such a sentinel function would be expected to show negative relationships to alpha power. ICs 5, 22 and 8 showed a negative relationship to alpha power, consistent with a sentinel function. As can be seen in Figure 4, these networks overlap with the proposed 'introspection' network of IC11 but do encompass other regions. These results, showing spatially overlapping components that have both positive and negative relationships to alpha power, highlight the DMN's functional duality and confirm that tissue within the same voxels can support distinct functional roles. Further, the regions of strongest overlap (white areas in Figure 4, including MPFC and PCC) may be key locations involved in integrating or switching between the DMN's introspective and sentinel functions.

This switching between internal and external locus of attention is essential to regulating our conscious experience (Mantini et al. , 2013). Pathology affecting the DMN, in particular the MPFC and PCC, would then be expected to have negative implications for

attention, spontaneous thought, and consciousness. Such a link has been found between a disruption in PCC activity and disorders of consciousness when compared to healthy controls (Crone et al. , 2015). Deactivations in regions of the DMN, particularly the PCC, have also been found following spike-and-wave discharges in patients with idiopathic generalized epilepsy, accompanied by altered or loss of consciousness (Gotman et al, 2005). Previous work has also shown decreased cerebral blood flow to DMN regions in patients with impaired consciousness during generalized tonic-clonic seizures (Blumenfeld et al, 2009). In this context, decreased activity in the overlapping regions of IC5 and IC11 (MPFC and PCC) may then be interpreted as an interruption of the sentinel and introspective modes of the DMN, resulting in the observed states of altered consciousness. This may imply an internal "push-pull" relationship to the modes of the DMN in addition to that put forth in the "network inhibition hypothesis" between the DMN and sub-cortical structures (Danielson et al, 2011).

To conclude, we have shown, using group ICA applied to fMRI, that the default mode network can be decomposed into independent sub-networks. These sub-networks are partially overlapping, and have both positive and negative correlations with EEG-recorded alpha power. The fact that the DMN can be decomposed into sub-networks with differing correlations with EEG alpha power may explain much of the inconsistency in previous studies looking to examine the link between the DMN and alpha power. The MPFC and the PCC are sites of overlap of two sub-networks that have opposite correlations with EEG alpha power, indicating their different proposed functions (sentinel vs. introspection). These data also suggest that the regions of overlap of networks may be involved in switching between introspection and sentinel functions.

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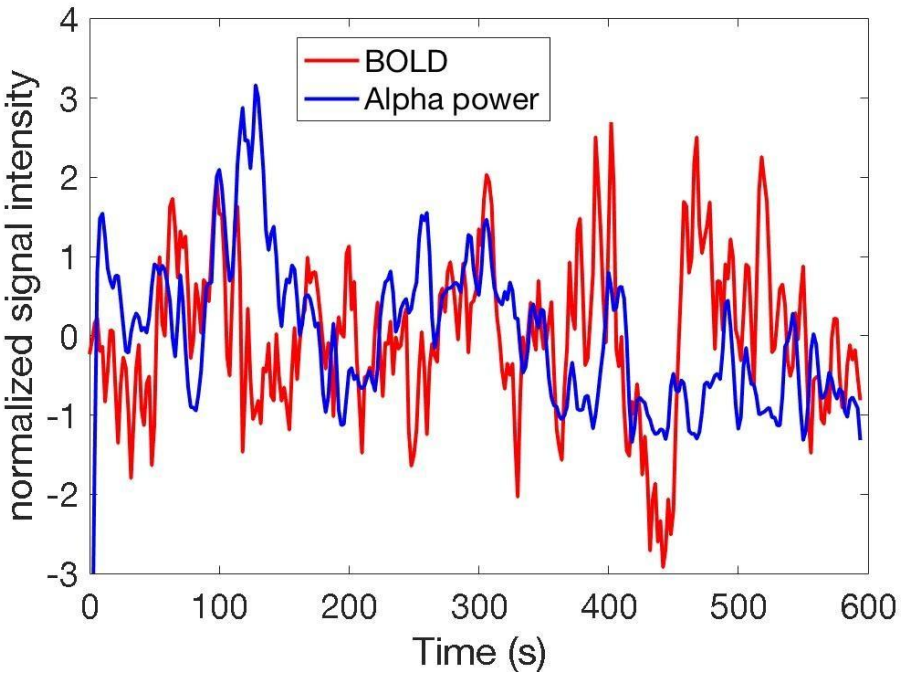

Figure 1: For illustration, we show a BOLD time course for IC11 in red for a representative participant. In blue is the alpha time course for the same participant's data. To fit these images to the same plot, both time courses are normalized by their standard deviation. Note that the alpha time course represents alpha power averaged over a 2- second window and then convolved with a function to account for the hemodynamic delay. The resulting time course was used to identify the correlation between the BOLD signal and alpha oscillations. Also note that IC11 includes orbital and medial prefrontal regions coupled with posterior cingulate cortex. This was the only IC that exhibited a positive correlation to alpha power ($p = 0.0192$).

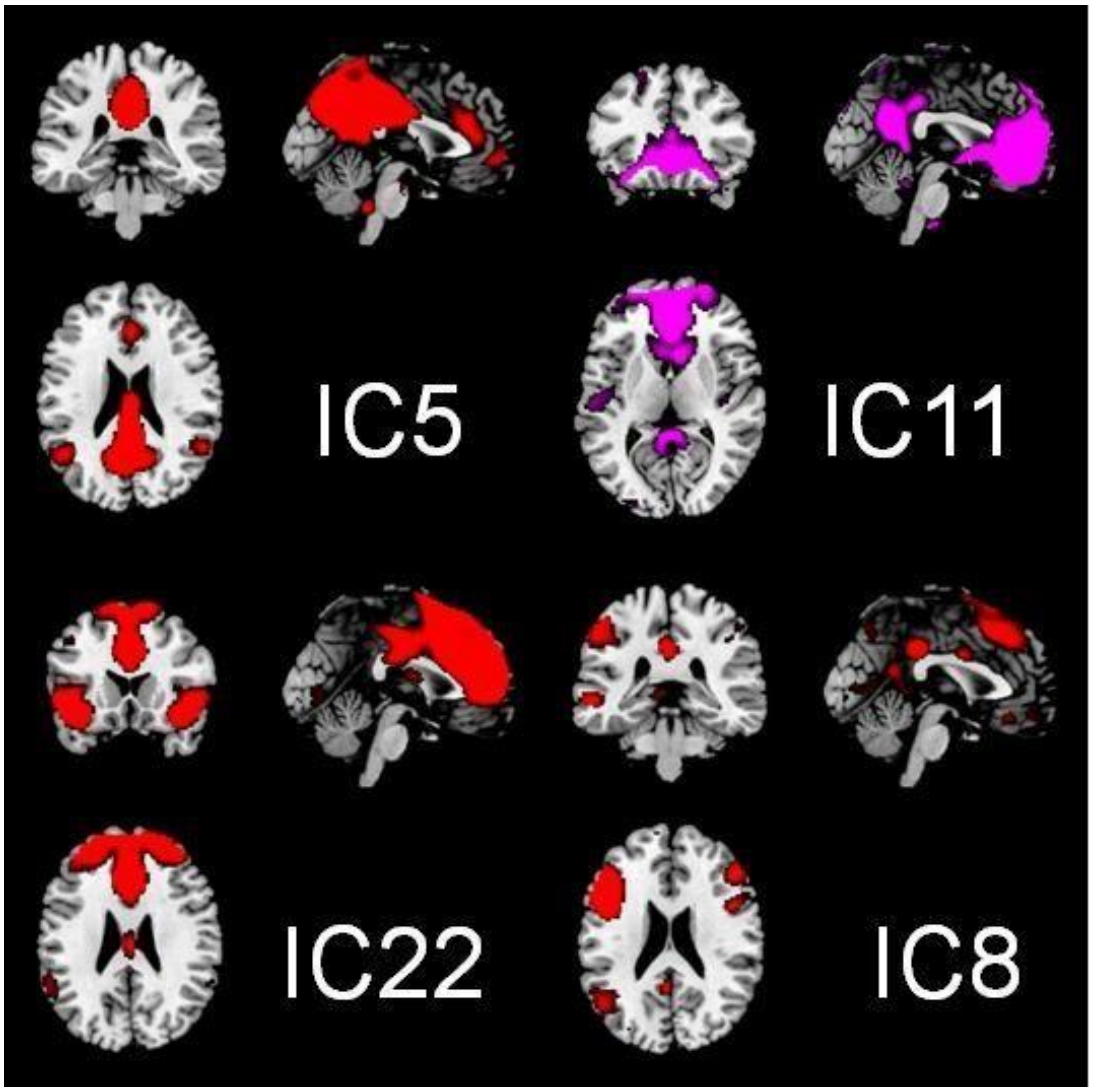

Figure 2: Group level independent components containing DMN regions significantly correlated with alpha. Negative correlations in red, positive correlations in violet. IC5: Posterior cingulate and parietal cortex, negative correlation ($p = 0.0336$). IC11: Orbital and medial prefrontal regions coupled with posterior cingulate cortex, positive correlation ($p = 0.0192$). IC22: Thalamus, medial frontal and bilateral temporal activations, negative correlation ($p = 0.0216$). IC8: Bilateral, lateral and superior frontal and cingulate cortex, negative correlation ($p = 0.0185$).

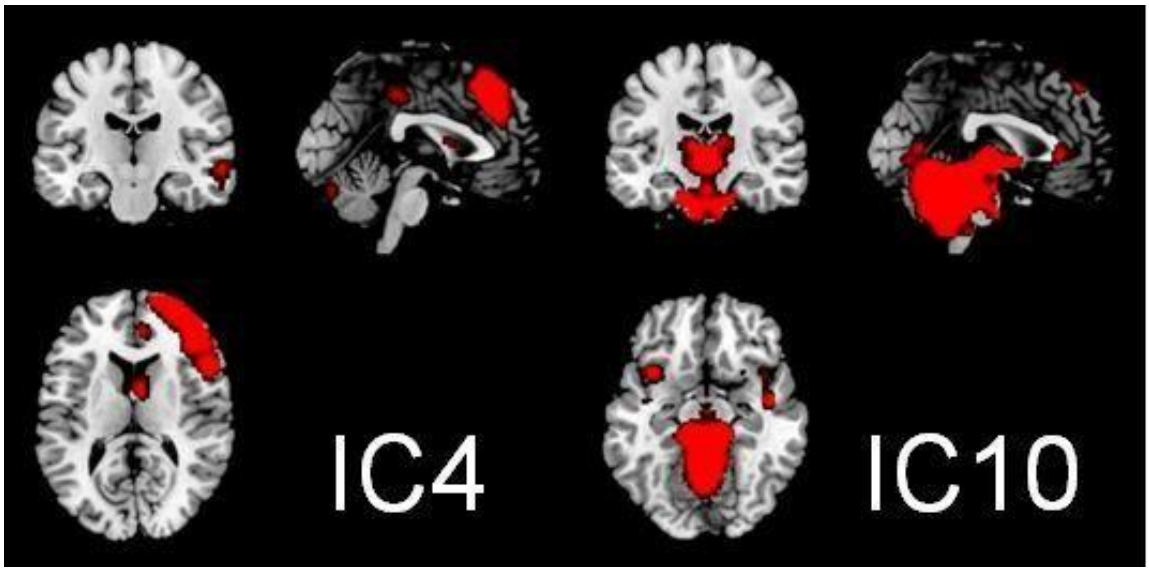

Figure 3: Group level independent components significantly correlated with alpha (non-DMN components). Negative correlations in red. IC4: Right frontal and right temporal regions ($p = 0.0195$). IC10: Cerebellum and brain stem ($p = 0.0084$).

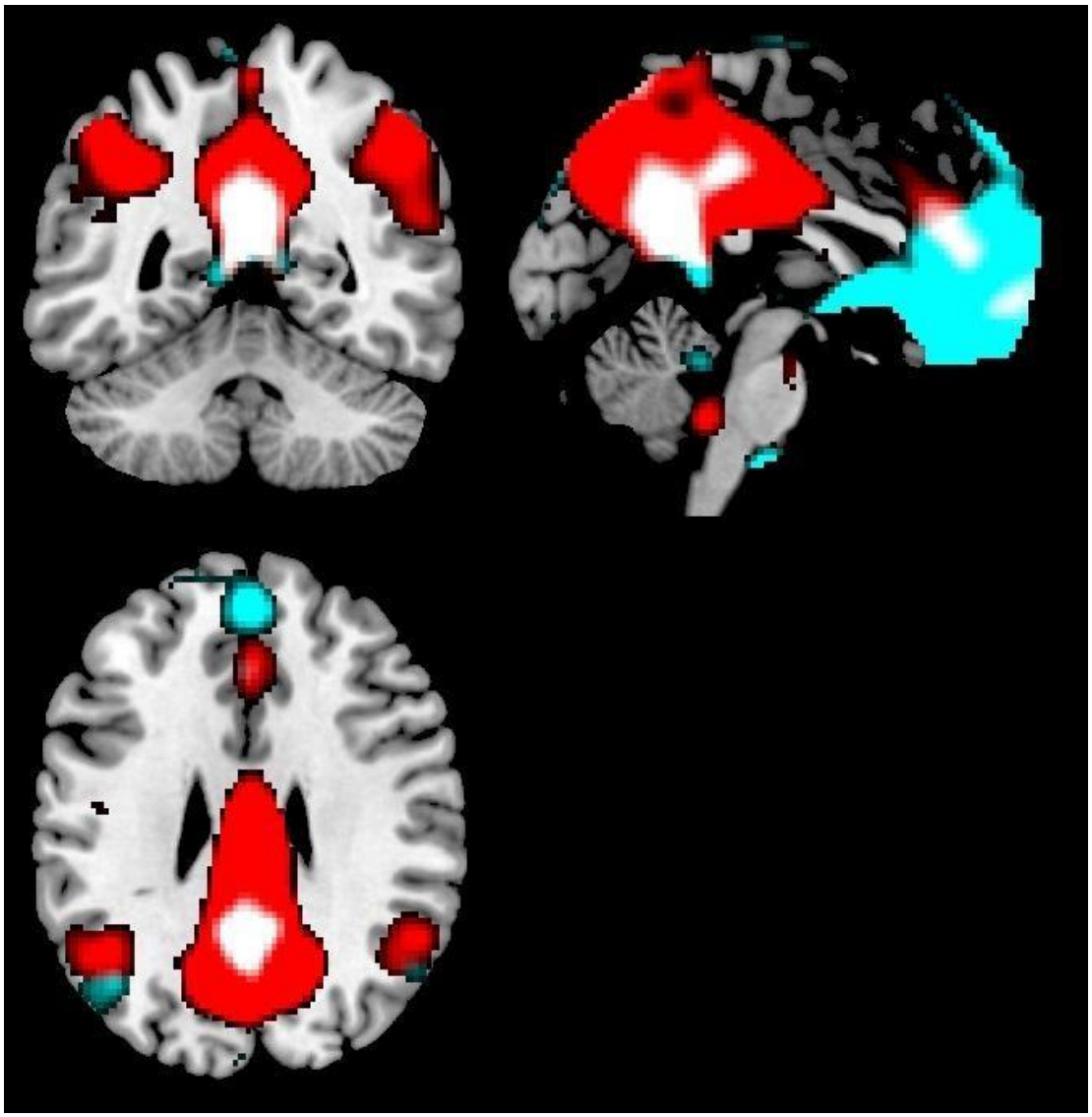

Figure 4: Composite overlay showing overlap (white) of IC11 (cyan) and IC5 (red).

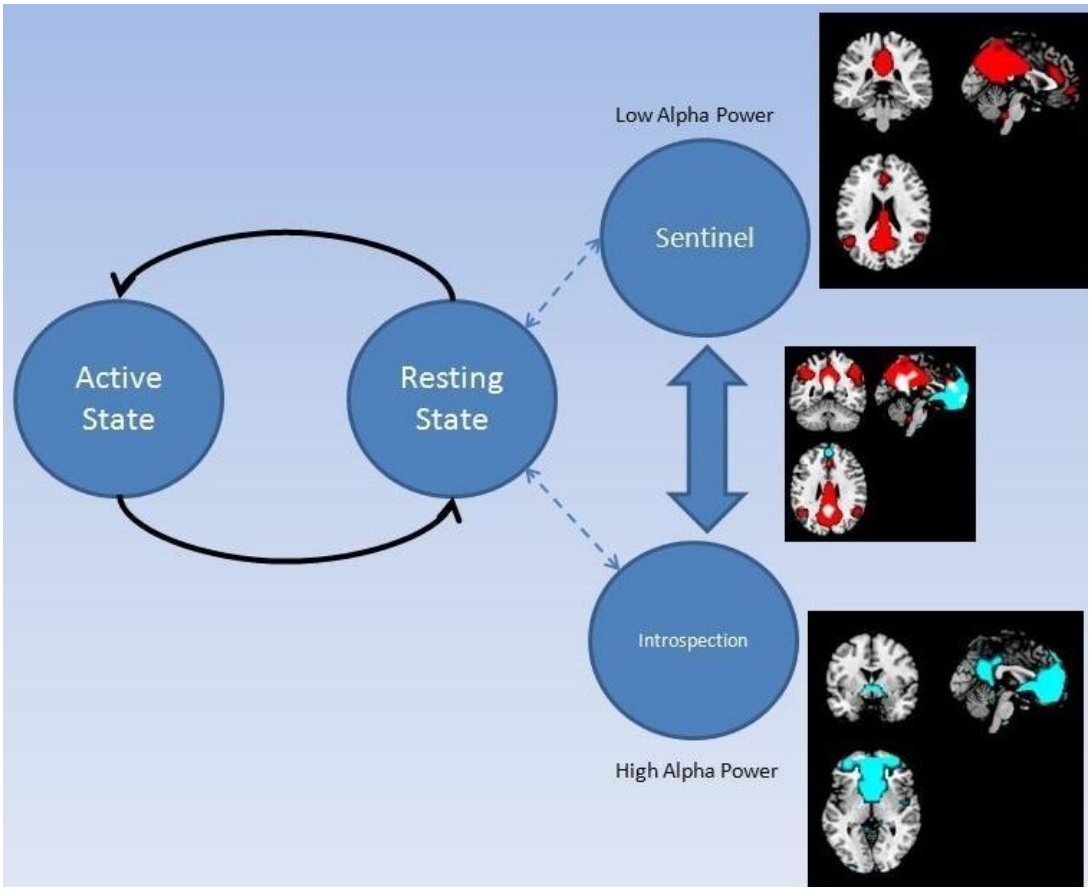

Figure 5: Diagram showing DMN function toggling between sentinel and introspective states correlated with low and high alpha power. Associated independent components based on their correlation with alpha power are shown to the right, IC5 above and IC11 below.

Table 1: All independent components of the BOLD signal with a significant relationship to alpha power. Independent components are listed, followed by indication of whether the component was judged to be a part of the DMN, a rough description of the brain regions encompassed by the IC, the sign of the correlation with alpha power, and a p-value of that effect.

IC	**DMN?**	**Brain Region**	**Sign of correlation with alpha power**	**p-value**
IC4	Not DMN	Right frontal and right temporal cortex	**Negative**	0.02
IC 5	DMN	Posterior Cingulate and parietal cortex	**Negative**	0.03
IC8	DMN	Superior frontal and cingulate cortex	**Negative**	0.02
IC10	Not DMN	Cerebellum and brain stem	**Negative**	0.01
IC11	DMN	Orbital and medial prefrontal regions, posterior cingulate	**Positive**	0.02
IC22	DMN	Thalamus, medial frontal and bilateral temporal	**Negative**	0.02

CONCLUSION

Using ICA applied to fMRI data obtained concurrently with continuous scalp EEG data, we have shown that the default mode network can be decomposed into independent sub-networks. Some of these sub-networks have spatial overlaps and have both positive and negative correlations with alpha power. This separation into sub-networks may explain some of the inconsistency in previous studies which sought to clarify the relationship between the DMN and alpha power. We have also shown the MPFC and PCC are sites of overlap between two sub-networks which have opposite correlations with alpha power. While the opposite correlations indicate and support the introspective and sentinel hypotheses regarding the DMN (Mason et al., 2007, Raichle et al., 2001), these overlapping regions suggest involvement in the switching between these functions. Further study is warranted in determining the role these regions may play in conscious experience and pathologies which involve states of altered consciousness.

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APPENDIX

IRB APPROVAL LETTER

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Institutional Review Board for Human Use

Form 4: IRB Approval Form
Identification and Certification of Research
Projects Involving Human Subjects

UAB's Institutional Review Boards for Human Use (IRBs) have an approved Federalwide Assurance with the Office for Human Research Protections (OHRP). The Assurance number is FWA00005960 and it expires on November 8, 2021. The UAB IRBs are also in compliance with 21 CFR Parts 50 and 56.

Principal Investigator:	SZAFLARSKI, JERZY P
Co-Investigator(s):	ALLENDORFER, JANE B DEWOLFE, JENNIFER L VER HOEF, LAWRENCE W
Protocol Number:	**X130109003**
Protocol Title:	*Combined EEG/fMRI in Patients with Focal Onset Seizures*

The IRB reviewed and approved the above named project on 12/13/16. The review was conducted in accordance with UAB's Assurance of Compliance approved by the Department of Health and Human Services. This Project will be subject to Annual continuing review as provided in that Assurance.

This project received EXPEDITED review.

IRB Approval Date: 10-13-16

Date IRB Approval Issued: 12/13/16

IRB Approval No Longer Valid On: 12/13/17

Marion Dorn

Expedited Reviewer
Member - Institutional Review Board
for Human Use (IRB)

Investigators please note:

The IRB approved consent form used in the study must contain the IRB approval date and expiration date.

IRB approval is given for one year unless otherwise noted. For projects subject to annual review research activities may not continue past the one year anniversary of the IRB approval date.

Any modifications in the study methodology, protocol and/or consent form must be submitted for review and approval to the IRB prior to implementation.

Adverse Events and/or unanticipated risks to subjects or others at UAB or other participating institutions must be reported promptly to the IRB.

470 Administration Building
701 20th Street South
205.934.3789
Fax 205.934.1301
irb@uab.edu

The University of
Alabama at Birmingham
Mailing Address:
AB 470
1720 2ND AVE S
BIRMINGHAM AL 35294-0104

Informed Consent Document – Epilepsy Participant

TITLE OF RESEARCH: Combined EEG/fMRI in patients with focal onset seizures

IRB PROTOCOL: X130109003

INVESTIGATOR: Dr. Jerzy Szaflarski

SPONSOR: Department of Neurology

PARTIAL SUPPORT: Neuroscan Compumedics, Inc

Purpose of the Research

You are being asked to take part in this research study because you are between the age of 18 and 65 years of age and you are considering surgery for your treatment resistant epilepsy. Your participation will allow us to obtain valuable EEG (Electroencephalography) and fMRI (functional magnetic resonance imaging) data as it relates to epilepsy pre-surgical evaluation.

The purpose of this study is to determine if the location of where electrical discharges begin in the brain can be found through EEG/fMRI during presurgical evaluation in order to increase seizure-free outcomes after surgery.

A total of about 50 patients will take part in this study at the University of Alabama at Birmingham. Approximately 25 healthy controls and approximately 25 patients with treatment resistant epilepsy will participate. You will have two research study visits. The screening visit will last approximately 1.5 hours and your return visit will last approximately 1 hour.

The Principal Investigator may decide to remove you from this research study at any time if you cannot understand or follow the procedures required to complete the study. You may withdraw from the study at any time.

Explanation of Procedures

After you have had time to read this consent form and have had all of your questions answered by Dr. Szaflarski or other study personnel and you decide to take part in this study, you will sign this consent form and then the following procedures will be performed.

At your screening visit, you will be asked about your medical history including any surgeries that you have had, any medical illnesses, medications that you are currently taking and if you have ever had a seizure.

You will have a concurrent functional MRI (fMRI) scan and an EEG performed prior to your standard of care surgery. The fMRI, which is a procedure that has been approved by the FDA, is similar to the standard MRI with the exception that during this study you will be asked to wear an EEG cap. The EEG cap is made of an elastic fabric that is fitted securely over your head during the scan.

The MRI technologist or study staff will perform a standard safety screening. He/she will go through a checklist with you of your medical history and safety questions used in routine medical MRI

scanning. If you are a woman able to have children and you have not recently had a pregnancy screening as a part of standard of care in the Epilepsy Monitoring Unit, you will have a urine pregnancy test prior to your MRI visits.

Before each scan, EEG electrodes will be applied via a MagLink EEG cap that is placed on your head. An approximately 10 minute long EEG sample will be obtained before the next step. Next, with the EEG cap in place, you will be escorted to the scanner and placed inside it. MRI scanning will then proceed and take approximately 45-60 minutes. Once you have completed the scanning session you will be removed from the scanner.

Approximately 6-8 weeks after your surgery, you will have a structural MRI obtained without the use of the MagLink EEG cap. Additional prior standard of care information including your medical history, imaging data and neuropsychological testing will be collected by Dr. Szaflarski or members of his research staff by interview and medical records review.

You will be in the study for approximately 2 months.

Risks and Discomforts

Risks involved in this study are minimal. There may be some irritation of the scalp caused by the EEG cap and/or gel. There may be some discomfort due to noise produced by the magnetic resonance scanner. Also, during the imaging, subjects occasionally may become claustrophobic (afraid of closed/narrow spaces). Any person who experiences discomfort or distress will be immediately removed from the scanner.

The MRI scan and EEG are performed for research purposes only and will not be reviewed by any physicians at UAB for clinical findings. The type of MRI scan and EEG that you will have, have been designed primarily for research purposes and may not be ideal for diagnosing other problems. However, if we believe that we have found a medical problem in your MRI scan or EEG, we will contact you and will help you get medical follow-up for the problem. If you are interested, you can request that a copy of your MRI scan or EEG be sent to your own physician for review. We can provide an electronic copy at no charge. You must provide us with a separate signed authorization for release of the scan.

Please initial below:
_____ I have read the information above, or it has been read to me, and I have had the chance to ask questions.

There is also a small possibility that the radiofrequency waves used in this study may cause peripheral nerve stimulation (your hand or leg may jump).

Another potential risk includes loss of confidentiality. To protect you from this risk, all of your health and personal information will be coded and kept in a password-protected database or

in a secure cabinet with access only to study staff. Precautions are in place to minimize any loss of confidentiality.

Alternatives

The alternative to participating in this study is to not participate. If you decide not to participate in this study, there will be no change in your treatment.

Benefits

There is no guarantee that the study will help you. The investigators hope the information learned from this research study will benefit other patients with epilepsy in the future.

Information for Women of Childbearing Potential

If you are a woman able to have children, you will not participate in this research study unless you have a negative pregnancy test before your MRI scans.

Confidentiality

Information obtained about you for this study will be kept confidential to the extent allowed by law. Research information that identifies you may be shared with the UAB Institutional Review Board (IRB) and others who are responsible for ensuring compliance with laws and regulations related to research, including people on behalf of the Department of Neurology; and the Office for Human Research Protections (OHRP). The results of the study may be published for scientific purposes. These results could include your EEG tests and MRI scans. However, your identity will not be given out.

Results of your EEG/fMRI will be shared with Neuroscan Compumedics, Inc but your identity will not be given out.

Voluntary Participation and Withdrawal

Whether or not you take part in this study is your choice. There will be no penalty if you decide not to be in the study. If you decide not to be in the study, you will not lose any benefits you are otherwise owed. You are free to withdraw from this research study at any time. Your choice to leave the study will not affect your relationship with this institution.

You may be removed from the study without your consent if the sponsor ends the study, if the study doctor decides it is not in the best interest of your health, or if you are not following the study rules.

If you are a UAB student or employee, taking part in this research is not a part of your UAB class work or duties. You can refuse to enroll, or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research.

Cost of Participation

There will be no cost to you for taking part in this study. All tests, scans, and medical care related to this study will be provided to you at no cost during the study period. The costs of your standard medical care will be billed to you and/or your insurance company in the usual manner.

Payment for Participation in Research

You will be paid $25 for each study visit for a total of $50 within 2 weeks of your study visits. Ask the study staff about the method of payment that will be used for this study (e.g., check, cash).

Significant New Findings

You will be told by your doctor or the study staff if new information becomes available that might affect your choice to stay in the study.

Payment for Research-Related Injuries

UAB has not provided for any payment if you are harmed as a result of taking part in this study. If such harm occurs, treatment will be provided. However, this treatment will not be provided free of charge.

Questions

If you have any questions, concerns, or complaints about the research or a research- related injury including available treatments, please contact Dr. Jerzy Szaflarski. He will be glad to answer any of your questions. Dr. Szaflarski's number is 205-934-3866. Dr. Szaflarski may also be reached after hours by paging him at 205-934-3411 (beeper 6816).

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll free at 1-855-860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday. You may also call this number in the event the research staff cannot be reached or you wish to talk to someone else.

Legal Rights

You are not waiving any of your legal rights by signing this informed consent document.

Signatures

Your signature below indicates that you agree to participate in this study. You will receive a copy of this signed document.

Signature of Participant	Date
Signature of Witness	Date
Signature of Person Obtaining Informed Consent Document	Date

University of Alabama at Birmingham
AUTHORIZATION FOR USE/DISCLOSURE OF
PROTECTED HEALTH INFORMATION (PHI) FOR RESEARCH

Participant Name:_____
Research Protocol: Combined EEG/fMRI in patients with focal onset seizures

UAB IRB Protocol Number: X130109003
Principal Investigator: Jerzy Szaflarski, MD, PhD
Sponsor:Department of Neurology
Partial Support: Neuroscan Compumedics, Inc

What is the purpose of this form? You are being asked to sign this form so that UAB may use and release your protected health information for research. Participation in research is voluntary. If you choose to participate in the research, you must sign this form so that your protected health information may be used for the research.

Why do the researchers want my protected health information? The researchers want to use your protected health information as part of the research protocol listed above and as described to you in the informed consent.

What protected health information do the researchers want to use? All medical information, including but not limited to information and/or records of any diagnosis or treatment of disease or condition, which may include sexually transmitted diseases (e.g., HIV, etc.) or communicable diseases, drug/alcohol dependency, etc.; all personal identifiers, including but not limited to your name, social security number, medical record number, date of birth, dates of service, etc.; any past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of whatever kind, including but not limited to drug/alcohol treatment, psychiatric/psychological treatment; financial/billing information, including but not limited to copies of your medical bills, and any other information related to or collected for use in the research protocol, regardless of whether the information was collected for research or non-research (e.g., treatment) purposes.

Who will disclose, use and/or receive my protected health information? All individuals/entities listed in the informed consent documents, including but not limited to, the physicians, nurses and staff and others performing services related to the research (whether at UAB or elsewhere); other operating units of UAB, HSF, UAB Highlands, Children's of Alabama, Eye Foundation Hospital, and the Jefferson County Department of Health, as necessary for their operations; the IRB and its staff; the sponsor of the research and its employees and agents, including any CRO; and any outside regulatory agencies, such as the Food and Drug Administration, providing oversight or performing other legal and/or regulatory functions for which access to participant information is required.

How will my protected health information be protected once it is given to others? Your protected health information that is given to the study sponsor will remain private to the extent possible, even though the study sponsor is not required to follow the federal privacy laws. However, once your information is given to other organizations that are not required to follow federal privacy laws, we cannot assure that the information will remain protected.

How long will this Authorization last? Your authorization for the uses and disclosures described in this Authorization does not have an expiration date.

Can I cancel this Authorization? You may cancel this Authorization at any time by notifying the Principal Investigator, in writing, referencing the research protocol and IRB Protocol Number. If you cancel this Authorization, the study doctor and staff will not use any new health information for research. However, researchers may continue to use the protected health information that was provided before you cancelled your authorization.

Can I see my protected health information? You have a right to request to see your protected health information. However, to ensure the scientific integrity of the research, you will not be able to review the research information until after the research protocol has been completed.

Signature of participant: _____ Date: _____

or participant's legally authorized representative: _____ Date: _____

Printed Name of participant's representative: _____

Relationship to the participant: _____

Informed Consent Document – Control

TITLE OF RESEARCH: Combined EEG/fMRI in patients with focal onset seizures

IRB PROTOCOL: X130109003

INVESTIGATOR: Dr. Jerzy Szaflarski

SPONSOR: Department of Neurology

PARTIAL SUPPORT: Neuroscan Compumedics, Inc

Purpose of the Research

You are being asked to take part in this research study because you are between the age of 18 and 65 years of age and are a healthy individual. Your participation will allow us to obtain valuable EEG (Electroencephalography) and fMRI (functional magnetic resonance imaging) data as it relates to epilepsy pre-surgical evaluation.

The purpose of this study is to determine if the location of where electrical discharges begin in the brain can be found through EEG/fMRI during presurgical evaluation in order to increase seizure-free outcomes after surgery.

A total of about 50 patients will take part in this study at the University of Alabama at Birmingham. Approximately 25 healthy controls and 25 patients with treatment resistant epilepsy will participate. You will have one research study visit that will last approximately 1.5 hours.

The Principal Investigator may decide to remove you from this research study at any time if you cannot understand or follow the procedures required to complete the study. You may withdraw from the study at any time.

Explanation of Procedures

After you have had time to read this consent form and have had all of your questions answered by Dr. Szaflarski or other study personnel and you decide to take part in this study, you will sign this consent form. The following study procedures will be performed.

At your visit, you will be asked about your medical history including any surgeries that you have had, any medical illnesses, medications that you are currently taking and if you have ever had a seizure.

You will have a concurrent functional MRI (fMRI) scan and an EEG performed. The fMRI, which is a procedure that has been approved by the FDA, is similar to the standard MRI with the exception that during this study you will be asked to wear an EEG cap. The EEG cap is made of an elastic fabric that is fitted securely over your head during the scan.

The MRI technologist or study staff will perform a standard safety screening. He/she will go through a checklist with you of your medical history and safety questions used in routine medical MRI scanning. If you are a woman able to have children, you will have a urine pregnancy test prior to your MRI visit.

Before each scan, EEG electrodes will be applied via a MagLink EEG cap that is placed on your head. An approximately 10 minute long EEG sample will be obtained before the next step. Then, with the EEG cap in place, you will be escorted to the scanner and placed inside it. MRI scanning will then proceed and take approximately 45-60 minutes. Once you have completed the scanning session you will be removed from the scanner.

Risks and Discomforts

Risks involved in this study are minimal. There may be some irritation of the scalp caused by the EEG cap and/or gel. There may be some discomfort due to noise produced by the magnetic resonance scanner. Also, during the imaging, subjects occasionally may become claustrophobic (afraid of closed/narrow spaces). Any person who experiences discomfort or distress will be immediately removed from the scanner.

The MRI scan and EEG are performed for research purposes only and will not be reviewed by any physicians at UAB for clinical findings. The type of MRI scan and EEG that you will have, have been designed primarily for research purposes and may not be ideal for diagnosing other problems. However, if we believe that we have found a medical problem in your MRI scan or EEG, we will contact you and will help you get medical follow-up for the problem. If you are interested, you can request that a copy of your MRI scan or EEG be sent to your own physician for review. We can provide an electronic copy at no charge. You must provide us with a separate signed authorization for release of the scan.

Please initial below:
_____ I have read the information above, or it has been read to me, and I have had the chance to ask questions.

There is also a small possibility that the radiofrequency waves used in this study may cause peripheral nerve stimulation (your hand or leg may jump).

Another potential risk includes loss of confidentiality. To protect you from this risk, all of your health and personal information will be coded and kept in a password-protected database or in a secure cabinet with access only to study staff. Precautions are in place to minimize any loss of confidentiality.

Alternatives

The alternative to participating in this study is to not participate.

Benefits

There is no benefit to you, as a healthy control, for participation in the study. The investigators hope the information learned from this research study will benefit patients with epilepsy in the future.

Information for Women of Childbearing Potential

If you are a woman able to have children, you will not participate in this research study unless you have a negative pregnancy test before your MRI scan.

Confidentiality

Information obtained about you for this study will be kept confidential to the extent allowed by law. Research information that identifies you may be shared with the UAB Institutional Review Board (IRB) and others who are responsible for ensuring compliance with laws and regulations related to research, including people on behalf of the Department of Neurology; and the Office for Human Research Protections (OHRP). The results of the study may be published for scientific purposes. These results could include your EEG test and MRI scan. However, your identity will not be given out.

Results of your EEG/fMRI will be shared with Neuroscan Compumedics, Inc but your identity will not be given out.

Voluntary Participation and Withdrawal

Whether or not you take part in this study is your choice. There will be no penalty if you decide not to be in the study. If you decide not to be in the study, you will not lose any benefits you are otherwise owed. You are free to withdraw from this research study at any time. Your choice to leave the study will not affect your relationship with this institution.

You may be removed from the study without your consent if the sponsor ends the study, if the study doctor decides it is not in the best interest of your health, or if you are not following the study rules.

If you are a UAB student or employee, taking part in this research is not a part of your UAB class work or duties. You can refuse to enroll, or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research.

Cost of Participation

There will be no cost to you for taking part in this study. The EEG/fMRI will be provided to you at no cost during the study period.

Payment for Participation in Research

You will be paid $25 for your study visit within 2 weeks of your study visit. Ask the study staff about the method of payment that will be used for this study (e.g., check, cash).

Significant New Findings

You will be told by your doctor or the study staff if new information becomes available and might affect your choice to stay in the study.

Payment for Research-Related Injuries

UAB has not provided for any payment if you are harmed as a result of taking part in this study. If such harm occurs, treatment will be provided. However, this treatment will not be provided free of charge.

Questions

If you have any questions, concerns, or complaints about the research or a research-related injury including available treatments, please contact Dr. Jerzy Szaflarski. He will be glad to answer any of your questions. Dr. Szaflarski's number is 205-934-3866. Dr. Szaflarski may also be reached after hours by paging him at 205-934-3411 (beeper 6816).

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll free at 1-855-860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday. You may also call this number in the event the research staff cannot be reached or you wish to talk to someone else.

Legal Rights

You are not waiving any of your legal rights by signing this informed consent document.

Signatures

Your signature below indicates that you agree to participate in this study. You will receive a copy of this signed document.

Signature of Participant Date

Signature of Witness Date

Signature of Person Obtaining Informed Consent Document Date

University of Alabama at Birmingham
AUTHORIZATION FOR USE/DISCLOSURE OF
PROTECTED HEALTH INFORMATION (PHI) FOR RESEARCH

Participant Name:_____
Research Protocol: Combined EEG/fMRI in patients with focal onset seizures

UAB IRB Protocol Number: X130109003
Principal Investigator: Jerzy Szaflarski, MD, PhD
Sponsor: Department of Neurology
Partial Support: Neuroscan Compumedics, Inc

What is the purpose of this form? You are being asked to sign this form so that UAB may use and release your protected health information for research. Participation in research is voluntary. If you choose to participate in the research, you must sign this form so that your protected health information may be used for the research.

Why do the researchers want my protected health information? The researchers want to use your protected health information as part of the research protocol listed above and as described to you in the informed consent.

What protected health information do the researchers want to use? All medical information, including but not limited to information and/or records of any diagnosis or treatment of disease or condition, which may include sexually transmitted diseases (e.g., HIV, etc.) or communicable diseases, drug/alcohol dependency, etc.; all personal identifiers, including but not limited to your name, social security number, medical record number, date of birth, dates of service, etc.; any past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of whatever kind, including but not limited to drug/alcohol treatment, psychiatric/psychological treatment; financial/billing information, including but not limited to copies of your medical bills, and any other information related to or collected for use in the research protocol, regardless of whether the information was collected for research or non-research (e.g., treatment) purposes.

Who will disclose, use and/or receive my protected health information? All individuals/entities listed in the informed consent documents, including but not limited to, the physicians, nurses and staff and others performing services related to the research (whether at UAB or elsewhere); other operating units of UAB, HSF, UAB Highlands, Children's of Alabama, Eye Foundation Hospital, and the Jefferson County Department of Health, as necessary for their operations; the IRB and its staff; the sponsor of the research and its employees and agents, including any CRO; and any outside regulatory agencies, such as the Food and Drug Administration, providing oversight or performing other legal and/or regulatory functions for which access to participant information is required.

How will my protected health information be protected once it is given to others? Your protected health information that is given to the study sponsor will remain private to the extent possible, even though the study sponsor is not required to follow the federal privacy laws. However, once your information is given to other organizations that are not required to follow federal privacy laws, we cannot assure that the information will remain protected.

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Can I see my protected health information? You have a right to request to see your protected health information. However, to ensure the scientific integrity of the research, you will not be able to review the research information until after the research protocol has been completed.

Signature of participant: _____ Date: _____

or participant's legally authorized representative: _____ Date: _____

Printed Name of participant's representative: _____

Relationship to the participant: _____

Project Revision/Amendment Form

irb

Form version: June 26, 2012

In MS Word, click in the white boxes and type your text; double-click checkboxes to check/uncheck.

- **Federal regulations require IRB approval before implementing proposed changes. See Section 14 of the IRB Guidebook for Investigators for additional information.**
- **Change means any change, in content or form, to the protocol, consent form, or any supportive materials (such as the Investigator's Brochure, questionnaires, surveys, advertisements, etc.). See Item 4 for more examples.**

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29740

1. Today's Date	12-16-16

2. Principal Investigator (PI)

Name (with degree)	Jerzy Szaflarski, MD	**Blazer ID**	szaflaj
Department	Neurology	**Division (if applicable)**	Epilepsy
Office Address	CIRC 312	**Office Phone**	934-3866
E-mail	szaflaj@uab.edu	**Fax Number**	

Contact person who should receive copies of IRB correspondence (Optional)

Name	Jennifer Mahaffey	**E-Mail**	jmahaffe@uab.edu
Phone	996-4030	**Fax Number**	996-4039
	Office Address (if different from PI)	**SC 350D, Zip 0017**	

3. UAB IRB Protocol Identification

3.a. Protocol Number X130109003

3.b. Protocol Title Combined EEG/fMRI in patients with focal onset seizures

3.c. Current Status of Protocol—Check ONE box at left; provide numbers and dates where applicable

- ☐ **Study has not yet begun** — **No participants, data, or specimens have been entered.**
- ☒ **In progress, open to accrual** — **Number of participants, data, or specimens entered:** 21
- ☐ **Enrollment temporarily suspended by sponsor**
- ☐ **Closed to accrual, but procedures continue as defined in the protocol (therapy, intervention, follow-up visits, etc.)**
  - **Date closed:**
  - **Number of participants receiving interventions:**
  - **Number of participants in long-term follow-up only:**
- ☐ **Closed to accrual, and only data analysis continues**
  - **Date closed:**
  - **Total number of participants entered:**

4. Types of Change

Check all types of change that apply, and describe the changes in Item 5.c. or 5.d. as applicable. To help avoid delay in IRB review, please ensure that you provide the required materials and/or information for each type of change checked.

- ☐ **Protocol revision (change in the IRB-approved protocol)**
  In Item 5.c., if applicable, provide sponsor's protocol version number, amendment number, update number, etc.
- ☐ **Protocol amendment (addition to the IRB-approved protocol)**
  In Item 5.c., if applicable, provide funding application document from sponsor, as well as sponsor's protocol version number, amendment number, update number, etc.
- ☒ **Add or remove personnel**
  In Item 5.c., include name, title/degree, department/division, institutional affiliation, and role(s) in research, and address whether new personnel have any conflict of interest. See "Change in Principal Investigator" in the IRB Guidebook if the principal investigator is being changed.
  - ☐ **Add graduate student(s) or postdoctoral fellow(s) working toward thesis, dissertation, or publication**
    In Item 5.c., (a) identify these individuals by name; (b) provide the working title of the thesis, dissertation, or publication; and (c) indicate whether or not the student's analysis differs in any way from the purpose of the research described in the IRB-approved HSP (e.g., a secondary analysis of data obtained under this HSP).
- ☐ **Change in source of funding; change or add funding**
  In Item 5.c., describe the change or addition in detail, include the applicable OSP proposal number(s), and provide a copy of the application as funded (or as submitted to the sponsor if pending). Note that some changes in funding may require a new IRB application.

☐ **Add or remove performance sites**
In Item 5.c., identify the site and location, and describe the research-related procedures performed there. If adding site(s), attach notification of permission or IRB approval to perform research there. Also include copy of subcontract, if applicable. If this protocol includes acting as the Coordinating Center for a study, attach IRB approval from any non-UAB site added.

☐ **Add or change a genetic component or storage of samples and/or data component—this could include data submissions for Genome-Wide Association Studies (GWAS)**
To assist you in revising or preparing your submission, please see the IRB Guidebook for Investigators or call the IRB office at 934-3789.

☐ **Suspend, re-open, or permanently close protocol to accrual of individuals, data, or samples (IRB approval to remain active)**
In Item 5.c., indicate the action, provide applicable dates and reasons for action; attach supporting documentation.

☐ **Report being forwarded to IRB (e.g., DSMB, sponsor or other monitor)**
In Item 5.c., include date and source of report, summarize findings, and indicate any recommendations.

☐ **Revise or amend consent, assent form(s)**
Complete Item 5.d.

☐ **Addendum (new) consent form**
Complete Item 5.d.

☐ **Add or revise recruitment materials**
Complete Item 5.d.

☐ **Other (e.g., investigator brochure)**
Indicate the type of change in the space below, and provide details in Item 5.c. or 5.d. as applicable.
Include a copy of all affected documents, with revisions highlighted as applicable.

5. Description and Rationale

In Item 5.a. and 5.b, check Yes **or** No **and see instructions for** Yes **responses.**
In Item 5.c. and 5.d, describe—and explain the reason for—the change(s) noted in Item 4.

☐ Yes ☒ No **5.a. Are any of the participants enrolled as normal, healthy controls?**
If yes, describe in detail in Item 5.c. how this change will affect those participants.

☐ Yes ☒ No **5.b. Does the change affect subject participation, such as procedures, risks, costs, location of services, etc.?**
If yes, FAP-designated units complete a FAP submission and send to fap@uab.edu. Identify the FAP-designated unit in Item 5.c.
For more details on the UAB FAP, see www.uab.edu/cto.

5.c. Protocol Changes: In the space below, briefly describe—and explain the reason for—all change(s) to the protocol. ✓ Added in SIRB.

Adding Anthony Bowman back to study personnel. He was removed due to IRB training requirements but has not completed all necessary refresher training. Anthony is also using the data from this study towards his master's thesis, ""Relationship between alpha rhythm and the default mode network: An EEG-fMRI study." Anthony is a biomedical engineering student + has no conflicts w/the study. no COI

5.d. Consent and Recruitment Changes: In the space below,
(a) describe all changes to IRB-approved forms or recruitment materials and the reasons for them;
(b) describe the reasons for the addition of any materials (e.g., addendum consent, recruitment); and
(c) indicate either how and when you will reconsent enrolled participants or why reconsenting is not necessary (not applicable for recruitment materials).

Also, indicate the number of forms changed or added. For new forms, provide 1 copy. For revised documents, provide 3 copies:
- **a copy of the currently approved document (showing the IRB approval stamp, if applicable)**
- **a revised copy highlighting all proposed changes with "tracked" changes**
- **a revised copy for the IRB approval stamp.**

Signature of Principal Investigator [signature] Date 12/19/16

FOR IRB USE ONLY

☐ Received & Noted ☑ Approved Expedited* ☐ To Convened IRB

Signature (Chair, Vice-Chair, Designee) Date 12/22/16

DOLA 12/13/16

Change to Expedited Category Y / (N) / NA

*No change to IRB's previous determination of approval criteria at 45 CFR 46.111 or 21 CFR 56.111