#### **BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FIVE PAGES.** 

NAME: Morgan, Victoria Lee

#### eRA COMMONS USER NAME (credential, e.g., agency login): matangvl

#### POSITION TITLE: Professor of Radiology and Radiological Sciences

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Wright State University, Dayton, OH, USA	B.S.	08/1990	Biomedical Engineering
Vanderbilt University, Nashville, TN, USA	M.S.	05/1994	Biomedical Engineering
Vanderbilt University, Nashville, TN, USA	Ph.D.	12/1996	Biomedical Engineering

#### A. Personal Statement

In 2002, I became one of the first to apply functional MRI connectivity techniques to investigate networks in focal epilepsy (i). Since then, I have developed a research program focused on developing and applying methods to quantify networks in patients with epilepsy to better understand the effects of seizures on the brain. I hypothesized that network alterations could be used to identify and quantify seizure propagation pathways across the brain, which I believe is critical in understanding the behavioral and cognitive impairments associated with this disease (ii). This work was initially funded by an Epilepsy Foundation Research Grant and then by the NIH which resulted in the development of a method to detect regions of epileptic activity acting as nodes in the epileptic network. I applied these methods to examine relationships between functional connectivity across the identified epileptic networks and epilepsy status such as seizure frequency and duration of disease. I later expanded this to include other more advanced fMRI network analyses including Granger causality. Next, I investigated the relationship between MRI functional and diffusion based structural connectivity to predict short term (1 year) treatment outcomes after mesial temporal lobe epilepsy surgery. Currently, I have two NIH funded projects to characterize the evolution of functional and structural networks across the brain in temporal lobe epilepsy before and after surgical treatment. The ultimate goal of this work is to understand how network reorganization is related to anti-epileptic medication response, and to long term seizure recurrence after surgical treatment.

- i. <u>Morgan VL</u>, Abou-Khalil B, Modur P, Wushensky C, Price RR. MRI Functional Connectivity to Lateralize Temporal Lobe Epilepsy. *Tenth Scientific Meeting of the International Society for Magnetic Resonance in Medicine* 2002:1536.
- Englot DJ, Konrad PE, <u>Morgan VL</u>. Regional and global connectivity disturbances in focal epilepsy, related cognitive sequelae, and potential mechanistic underpinnings. *Epilepsia* 2016;57(10):1546-1557.
  <u>PMCID:PMC5056148</u>

### B. Positions and Honors

### **Positions and Employment**

1990-1992	Test Engineer, Impact Test Facility, Inland Fisher Guide Div., General Motors Corporation,
	Dayton, OH
1997	Consultant, Center for Cardiovascular Magnetic Resonance, Barnes-Jewish Hospital at
	Washington University Medical Center, St. Louis, MO
1997-1999	Sr. Research Assistant, Department of Radiology and Radiological Sciences, Vanderbilt
	University, Nashville, TN
1999-2000	Instructor, Department of Radiology and Radiological Sciences, Vanderbilt University,
	Nashville, TN
2000-2012	Assistant Professor, Department of Radiology and Radiological Sciences, Vanderbilt
	University, Nashville, TN
2008-2013	Assistant Professor, Department of Biomedical Engineering, Vanderbilt University,
	Nashville, TN
2012-2019	Associate Professor, Department of Radiology and Radiological Sciences, Vanderbilt
	University Medical Center, Nashville, TN
2019-Present	Professor, Department of Radiology and Radiological Sciences, Vanderbilt University
	Medical Center, Nashville, TN
2019-Present	Professor, Department of Biomedical Engineering, Vanderbilt University, Nashville, TN
2019-Present	Professor, Department of Neurology, Vanderbilt University Medical Center, Nashville, TN
2019-Present	Professor, Department of Neurological Surgery, Vanderbilt University Medical Center,
	Nashville

# **Other Experience and Professional Memberships**

2000-Present	Member, International Society of Magnetic Resonance in Medicine
2008-Present	Member, American Epilepsy Society
2010	Steering Committee on Imaging Science, National Academies Keck Futures Initiative
2011	Grant reviewer, NIH MEDI Study Section
2012-2014	NIH grant review panel, ad hoc reviewer
2014	ZMH1 ERB-C(09) R - BRAIN Initiative: Development and Validation of Novel Tools, NIH grant
	review panel, ad hoc reviewer
2014-2015	NOIT study section, NIH grant review panel, ad hoc reviewer
2014-2015	American Epilepsy Society, Scientific Program Committee
2014-20187	International Society of Magnetic Resonance in Medicine, Brain Function Study Group, Officer
2015-2019	NOIT study section, NIH grant review panel charter member
2017-present	International League Against Epilepsy (ILAE) Imaging Task Force of the Commission on
	Diagnostic Methods
2018	"My Brain Map" Workshop, Epilepsy Foundation

# <u>Honors</u>

Young Investigator's Bursary Award, International Epilepsy Congress, Lisbon, Portugal
 American Epilepsy Society Fellow
 Academy for Radiological and Biomedical Imaging Research, Distinguished Investigator
 Fellow of the American Institute for Medical and Biological Engineering

# C. Contributions to Science

1. Data driven fMRI methods for localization of the seizure focus and propagation network in focal epilepsy. As one of the first researchers to attempt to apply MRI functional connectivity mapping to the study of epileptogenic networks (abstract in 2002, award cited above), I found that the identification of the nodes of these networks would be a significant challenge. Some research institutions focused on the use of simultaneous EEG and MRI methods to localize interictal spikes presumed to be these nodes, but this technique is not widely available and remains clinically infeasible for many patients without frequent

interictal scalp EEG spiking. Therefore, I developed an fMRI data driven approach to identify the timing of interictal epileptic events called two-dimensional temporal clustering analysis (2dTCA). After some pilot study (1a), I validated the method on healthy controls (1b) and epilepsy patients (1c, 1d). This work has launched a field of data driven analyses of interictal epileptic fMRI data for both clinical and research purposes. I served as the primary investigator on the studies listed below. This work was funded by the Epilepsy Foundation (PI-Morgan) and an NIH R01 grant (PI-Morgan).

- 1a. <u>Morgan VL</u>, Li Y, Abou-Khalil B, Gore JC. Development of 2dTCA for detection of irregular, transient BOLD activity. *Human Brain Mapping*, 2008;29(1):57-69. <u>PMCID: PMC2719759</u>
- 1b. <u>Morgan, VL</u>, Gore, JC. Detection of irregular, transient fMRI activity in normal controls using 2dTCA: comparison to event-related analysis using known timing. *Human Brian Mapping* 2009;30:3393-3405. <u>PMCID: PMC2748174</u>
- Morgan, VL, Gore, JC, Abou-Khalil, B. Functional epileptic network in left mesial temporal lobe epilepsy detected using resting fMRI. *Epilepsy Research* 2010;88:168-178. <u>PMCID: PMC2823966</u>
- 1d. Maziero D, Velasco TR, Salmon CEG, <u>Morgan VL</u>. Two-dimensional temporal clustering analysis for patients with epilepsy: detecting epilepsy-related information in EEG-fMRI concordant, discordant and spike-less patients. *Brain Topography* 2018;31(2):322-336. <u>PMCID: PMC5884070</u>
- 2. MRI network connectivity alterations in epilepsy. After identifying potential nodes in temporal lobe epilepsy networks using methods including 2dTCA, my group focused on using MRI functional connectivity mapping to quantify changes in functional networks in patients with focal epilepsy. We related changes in hippocampal networks to memory function (2a) and uncovered potential compensation mechanisms in patients with preserved memory. We also related brainstem network alterations to several neurocognitive impairments (2b). In addition, we developed and applied novel image analysis methods to probe causal mechanisms (2c), and to identify specific oxygenation fluctuation frequencies of impairment in focal epilepsy (2d). I served as the primary investigator on the studies listed below. This work was funded through a NIH R01 grant (PI-Morgan).
  - 2a. Holmes MJ, Folley BS, Sonmezturk HH, Gore JC, Kang H, Abou-Khalil B, <u>Morgan VL</u>. Resting state functional connectivity of the hippocampus associated with neurocognitive function in left temporal lobe epilepsy. *Human Brain Mapping*, 2014;35(3):735-44. <u>PMCID:PMC3915042</u>
  - 2b. Englot DJ, D'Haese PF, Konrad PE, Jacobs ML, Gore JC, Abou-Khalil BW, <u>Morgan VL</u>. Functional connectivity disturbances of the reticular activating system in temporal lobe epilepsy. *Journal of Neurology, Neurosurgery and Psychiatry* 2017; 88(11):925-932. <u>PMCID:PMC5634927</u>
  - Morgan VL, Roger BP, Sonmezturk HH, Gore JC, Abou-Khalil B. Cross hippocampal influence in mesial temporal lobe epilepsy measured with high temporal resolution functional Magnetic Resonance Imaging. *Epilepsia* 2011;52(9):1741-1749. <u>PMCID:PMC4428312</u>
  - 2d. <u>Morgan VL</u>, Rogers BP, Abou-Khalil B. Segmentation of the thalamus based on BOLD frequencies affected in temporal lobe epilepsy. *Epilepsia* 2015;56(11):1819-27. <u>PMCID:PMC4626388</u>
- 3. **MRI network connectivity may improve prediction of treatment outcome.** Based on our previous experience in detecting alterations in networks in patients with focal epilepsy, we developed the hypothesis that network information, in addition to localization of the seizure focus, is required to more accurately predict seizure outcome after surgery. This is based on the premise that (1) networks evolve over time before and after treatment in unique ways across different individuals, and (2) that the state of these networks at the time of treatment and their evolution after treatment influences outcome. In a seminal work, we found that patients with unfavorable short-term (<1 year) outcome could be distinguished from those with favorable outcome using network characteristics, even when all other clinical characteristics were identical (3a). From there, we found that other networks in the contralateral hemisphere were predictive of long term (>1 year) outcome in these patients (3b). Finally, we began investigating post-surgical network evolution in these patients (3c) with the ultimate goal of using this information to predict even longer term outcomes. I served as the primary investigator on all of these studies listed below. This work is currently funded through two NIH R01 grants (PI-Morgan).
  - 3a. <u>Morgan VL</u>, Englot DJ, Rogers BP, Landman BA, Cakir A, Abou-Khalil BW, Anderson AW. Magnetic resonance imaging connectivity for the prediction of seizure outcome in temporal lobe epilepsy. *Epilepsia* 2017;58(7):1251-1260. <u>PMCID:PMC5498250</u>

- 3b. <u>Morgan VL</u>, Rogers BP, Anderson AW, Landman BA, Englot DJ. Divergent network properties that predict early surgical failure versus late recurrence in temporal lobe epilepsy. *Journal of Neurosurgery* 2019; April 5. <u>PMCID:PMC6778487 [Available 10-05-2020]</u>
- 3c. Morgan VL, Rogers BP, González HFJ, Goodale SE, Englot DJ. Characterization of post-surgical functional connectivity changes in temporal lobe epilepsy. *Journal of Neurosurgery* 2019; June 14 <u>PMCID:PMC6911037[Available 12-14-2020]</u>
- 4. **Structure-function relationships in the brain.** Elucidating the relationships between structure and function across the brain is critical is characterizing the evolution of the healthy brain and in those with chronic diseases. For this work I have collaborated with Zhaohua Ding, Ph.D. to design and implement MRI structural methodologies in healthy controls (4a), and then in the epileptic networks studied previously (4b). In epilepsy, we found that there was a linear relationship between functional connectivity and gray matter concentration in key nodes of these seizure networks which may be important in predicting the post-surgical outcome in these patients. In these two studies, I was the primary investigator. In our more recent collaboration (4c, 4d), I have supported Dr. Ding in his innovative development of spatio-temporal correlation tensors, which are a completely novel investigation of functional connectivity of white matter. My role in this work was to help determine validation procedures and to relate the findings to traditional functional connectivity methodologies. Currently, I am characterizing functional and structural network evolution before and after surgical treatment in focal epilepsy (funded by two NIH R01 grants PI-Morgan).
  - 4a. <u>Morgan VL</u>, Mishra A, Newton AT, Gore JC, Ding Z. Integrating Functional and Diffusion Magnetic Resonance Imaging for Analysis of Structure-Function Relationship in the Human Language Network. *PLoS ONE* 2009;4(8):E6660. doi:10.1371/journal.pone.0006660 <u>PMCID:PMC2721978</u>
  - 4b. Holmes MJ, Yang X, Landman BA, Ding Z, Kang H, Abou-Khalil BA, Sonmezturk HH, Gore JC, <u>Morgan VL</u>. Functional networks in temporal lobe epilepsy: a voxel-wise study of resting-state functional connectivity and gray matter concentration. *Brain Connectivity* 2013; 3(1):22-30. <u>PMCID:PMC3621340</u>
  - 4c. Ding Z, Newton AT, Xu R, Anderson AW, <u>Morgan VL</u>, Gore JC. Spatio-temporal correlation tensors reveal functional structure in human brain. *PLoS ONE* 2013; 8(12):e82107. <u>PMCID:PMC3855380</u>
  - 4d. Ding Z, Xu R, Bailey SK, Wu TL, <u>Morgan VL</u>, Cutting LE, Anderson AW, Gore JC. Visualizing functional pathways in the human brain using correlation tensors and Magnetic Resonance Imaging. *Magnetic Resonance Imaging* 2016;34(1):8-17. <u>PMCID PMC4714593</u>
- 5. Mild traumatic brain injury (mTBI). Recently I have worked to apply the MRI methods I developed for epilepsy to investigate mTBI. In one study I collaborated with the Vanderbilt athletic department to image varsity athletes within one week of sports concussion. That study determined an increase in cerebrovascular reactivity in these subjects over age-matched healthy controls (5a). This hyper-reactivity is similar to that detected in migraine, and may show the similarities between the two conditions. In the same study we found a linear relationship between functional connectivity and hyper-reactivity which suggests caution in interpreting functional connectivity measures in patient populations where the neurovascular coupling may be altered. In another study of adults with accidental mTBI, the normalization of thalamocortical functional connectivity was a strong indicator of improvement of pain scores and post-concussive symptoms after rehabilitation (5b).
  - 5a. Militana AR, Donahue MJ. Sills AK, Solomon GS, Gregory AJ, Strother MK, <u>Morgan VL</u>. Alterations in default-mode network connectivity may be influenced by cerebrovascular changes within one week of sports related concussion in college varsity athletes: a pilot study. *Brain Imaging and Behavior* 2016;10(2):559-568. <u>PMCID:PMC4644725</u>
  - 5b. Banks SD, Coronado RA, Clemons LR, Abraham CM, Pruthi S, Conrad BN, <u>Morgan VL</u>, Guillamondegui OD, Archer KR. Thalamic functional connectivity in mild traumatic brain injury: Longitudinal associations with patient-reported outcomes and neurophysiological tests. *Archives of Physical Medicine and Rehabilitation* 2016; 97(8):1254-61. <u>PMCID:PMC4990202</u>

# Complete List of Published Work in NCBI MyBibliography and Google Scholar:

https://www.ncbi.nlm.nih.gov/myncbi/1hwgAfiRt4g5y/bibliography/public/ https://scholar.google.com/citations?user=C9rStd0AAAAJ&hl=en h-index 30, i10-index 47

# D. Additional Information: Research Support and/or Scholastic Performance

# <u>ACTIVE</u>

#### 1R01 NS108445-01A1 (Morgan) 04/01/2019-03/31/2024 NINDS

### MRI Connectivity Biomarkers of Treatment Responses in Focal Epilepsy

The ultimate goal of this study is to develop Magnetic Resonance Imaging connectivity based biomarkers of individual treatment outcome prediction for patients with focal epilepsy. This would lead to increases in the success rate of potentially risky treatments, and more efficient clinical management of this common debilitating disorder.

1R01 NS110130-02 (Morgan) 09/30/2018-06/30/2024 NINDS

The Role of Network Connectivity in Post-Surgical Seizure Recurrence in Temporal Lobe Epilepsy The ultimate goal of this study is to develop imaging based biomarkers of individual surgical treatment outcome prediction for patients with temporal lobe epilepsy through the study of brain evolution after surgical treatment in these patients.

4R00 NS097618-03 (Englot) 09/01/2017 - 08/31/2020 NINDS

*Multimodal Mapping of Subcortical and Cortical Functional Network Disturbances in Focal Epilepsy* The present studies will use functional magnetic resonance imaging (fMRI) to measure interictal functional connectivity between subcortical activating structures and neocortex in preoperative focal epilepsy patients vs. controls. Interictal connectivity patterns will be related to disease and neurocognitive parameters. Dynamic changes in connectivity will be measured before, during, and after seizures using icEEG and related to consciousness impairing seizures..

1R01 NS112252-10 (Chang and Englot) 08/15/2019 – 05/31/2024 NINDS

Relating Vigilance to Connectivity and Neurocognition in Temporal Lobe Epilepsy

This project will use multimodal imaging to map vigilance in temporal lobe epilepsy and healthy control and its effect on network connectivity. This information will be related to neurocognitive function in these patients.

# **Recent Completed Research Support**

1R21 DC016080-01 (Wilson) 04/01/2017 - 03/31/2019 NIDCD

An Adaptive Semantic Paradigm for Valid and Reliable Language Mapping in Aphasia Studies on functional reorganization of language regions of the brain critically depend on the ability to identify language regions in individual patients and quantify any changes that take place over time. The absence of psychometrically sound language mapping paradigms that are feasible in individuals with aphasia is a significant roadblock to this research. The proposed study will develop an adaptive semantic matching paradigm that will provide a foundation for future research on neuroplasticity of language regions.

6R01 NS075270-06 (Morgan) 05/01/2016-02/28/2019 (NCE) NINDS

MRI Structural and Functional Connectivity Changes in Temporal Lobe Epilepsy

The overall goal of this project is to investigate and quantify the relationship between functional and structural network integrity in seizure propagation and language networks in TLE non-invasively using Magnetic Resonance Imaging (MRI); and to relate these network alterations to disease and cognitive characteristics before and after surgery. Both functional connectivity and structural connectivity will be measured in seizure propagation and language and memory networks of TLE patients prior to surgical treatment.

5R01NS035929-11 Binder (PI); Morgan (PI, Vanderbilt Site) NIH/NINDS Multi-site Study 12/1/12-110/31/16

Presurgical Applications of fMRI in Epilepsy

The goal of this study is to use functional MRI to predict cognitive outcome after left temporal lobe surgery for seizures.