BIOGRAPHICAL SKETCH

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NAME: Englot, Dario J.

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

POSITION TITLE: Associate Professor of Neurological Surgery, Neurology, Radiology, Computer Science, Electrical and Computer Engineering, and Biomedical Engineering; Director of Functional Neurosurgery and Surgical Director of Epilepsy; Vice Chair of Research and Innovation, Neurosurgery, Vanderbilt University

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
University of Scranton, Scranton, PA	B.S.	05/2003	Neuroscience
Yale University, New Haven, CT	M.Phil.	12/2007	Neuroscience
Yale University, New Haven, CT	Ph.D.	05/2009	Neuroscience
Yale University, New Haven, CT	M.D.	05/2010	Medicine
University of California, San Francisco, CA	Residency	06/2016	Neurological Surgery
Vanderbilt University, Nashville, TN	Fellowship	06/2017	Epilepsy Surgery and Functional Neurosurgery

A. Personal Statement

I have dedicated my professional life to research and treatment in the field of epilepsy, a common and devastating neurological disorder. My overarching research goal is to achieve a detailed understanding of brain network dysfunction in epilepsy, which will lead to novel treatment options including surgery, neuromodulation, and behavioral interventions. I have significant experience in neuroimaging and electrophysiology techniques in both humans and animal models, and in analysis methods to study brain connectivity in neurological disorders. Some of my interests include brain activity and connectivity disturbances related to arousal and cognitive networks, and how these relate to ictal loss of consciousness and interictal neuropsychological problems in epilepsy. I am also interested in brain network analyses that can improve upon current clinical strategies in epilepsy surgery, and make surgery more effective and less invasive. I have served as PI and co-I on independent NIH grants (R01, R00), as primary mentor (F31) on NIH training awards, and previously as a trainee grant recipient (F30, F32, K99). I have also received research support from the American Epilepsy Society and Epilepsy Foundation. My published bibliography includes >125 co-authored research papers in peer-reviewed journals, and >60 reviews/chapters/commentaries. I also currently serve as Chair of the Surgical Therapies Commission (2021-25) for the International League Against Epilepsy (ILAE).

Englot DJ, Hinkley LB, […], Kirsch HE, Nagarajan SS (2015) Global and regional functional connectivity maps of neural oscillations in focal epilepsy. Brain 138(8):2249-2262. PMC4840946.

Englot DJ, Gonzalez HJF, […], Landman BA, Morgan VL (2018) Relating structural and functional brainstem connectivity to disease measures in epilepsy. Neurology 91(1):e67-e77. PMC6091881.

Paulo DL, Wills KE, […],Narasimhan S, **Englot DJ** (2022) SEEG functional connectivity measures to identify epileptogenic zones: Stability, medication influence, and recording condition. Neurology 98(20):e2060-e2072. PMC9162047.

Johnson GW, Doss DJ, […],Wallace MT, **Englot DJ** (2023) The Interictal Suppression Hypothesis in focal epilepsy: Network-level supporting evidence. Brain 146(7):2828-2845. PMC10316780.

Relevant Current Research Support

NIH R01 NS134625 Englot (Role: PI) 12/06/2023-11/30/2028
Development of multimodal network analyses to improve epilepsy surgery outcomes
We will develop novel network neuroimaging and electrophysiology network measures to better define epileptogenic networks in surgical epilepsy and can ultimately be breaded applied broadly to improve care.

NIH R01 NS112252 Englot and Chang (Role: PI) 08/15/2019-05/31/2024
Relating vigilance to connectivity and neurocognition in temporal lobe epilepsy
Using simultaneous EEG, dynamic fMRI connectivity measurements, and psychometric testing, we will define networks underlying vigilance in healthy controls, and then probe these networks in epilepsy patients.

NIH R01 NS108445 Morgan (Role: Co-I) 02/15/2019-1/31/2025
MRI connectivity biomarkers of treatment response in focal epilepsy
The overall goal of this project is to develop and optimize MRI biomarkers of surgical and pharmacological treatment response in focal epilepsy by quantifying functional and structural networks across the brain.

NIH R01 NS1101130 Morgan (Role: Co-I) 09/30/2018-07/1/2024
The role of network connectivity in post-surgical seizure recurrence in temporal lobe epilepsy
The overall goal of this project is to quantify presurgical and post-surgical MRI network connectivity and their relationship to seizure recurrence after mesial temporal lobe surgery.

NIH R01 NS120518 Barth and Webster (Role: Co-I) 12/15/2020-11/30/2024
An MRI guided steerable needle to replace open brain surgery for epilepsy patients
The goal of this project is to develop novel minimally-invasive approaches to treat surgical epilepsy using a 3D-printed needle steering robot and MRI-guided delivery of thermal therapy.

NIH R01 AG060754 Constantinidis (Role: Co-I) 2/1/2019-1/31/2024
Primate model of deep brain stimulation for Alzheimer's and age-related cognitive decline
This project aims to define cognitive effects of deep brain stimulation (DBS) of the nucleus basalis of Meynert in aged non-human primate as a model for DBS for Alzheimer's disease.

Relevant Completed Research Support (past 3 years)

NIH K99/R00 NS097618 Englot (Role: PI) 07/01/2016-05/31/2021
Multimodal mapping of subcortical & cortical functional network disturbances in focal epilepsy
This project integrates electrophysiology and MRI techniques to define functional connectivity disturbances in surgical epilepsy patients, and examine the clinical implications of these brain network alterations.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2024-	Vice Chair of Research and Innovation, Dept. Neurological Surgery, Vanderbilt University
2022-	Associate Prof. of Neurological Surgery, Neurology, Radiology, Electrical Engineering, Computer Science, and Biomedical Engineering (with Tenure), Vanderbilt University
2020-	Director of Functional Neurosurgery, Vanderbilt University Medical Center
2017-	Assistant Prof. of Neurological Surgery, Vanderbilt University Medical Center
2017-	Faculty Affiliate, Vanderbilt Institute for Surgery and Engineering (VISE), Vanderbilt University Institute of Imaging Sciences (VUIIS), Vanderbilt Brain Institute (VBI), and Vanderbilt Kennedy Center (VKC)
2017-	Surgical Director of Epilepsy, Vanderbilt University Medical Center

Honors and Awards

2022	Grant W. Liddle Faculty Research Award, Vanderbilt University Medical Center
2019	Fellow of the American Assoc. of Neurological Surgeons (FAANS), Rolling Meadows, IL
2018	Fellow of the American Epilepsy Society (FAES), Washington, DC
2018	Kumar New Investigator Award, North Am Neuromodulation Soc (NANS), Las Vegas, NV
2017	Junior Scientist Award, North American Neuromodulation Society (NANS), Las Vegas, NV
2017	Travel Award, World Soc. for Stereotactic & Functional Neurosurgery (WSSFN), Berlin
2017	Reichert Award, World Soc. for Stereotactic & Functional Neurosurgery (WSSFN), Berlin
2016	Boldrey Award for Neuroscience, San Francisco Neurol Society (SFNS), Sonoma, CA
2016	Harold Rosegay Teaching Award, Dept. Neurological Surgery, UCSF

2015 Rosegay Award, Best Paper, San Francisco Neurological Society (SFNS), Monterey, CA
2015 First Place Poster in Functional, Amer Assoc Neurol Surgeons (AANS), Washington, DC
2015 Young Investigator Award, Amer Epilepsy Society (AES) Annual Meeting, Philadelphia, PA
2014-15 NRSA for Individual Postdoctoral Fellows (F32), NIH (NS086353)
2014 Best Research Presentation, CA Assoc. of Neurological Surgeons (CANS), Monterey, CA
2014 Harold Rosegay Teaching Award, Dept. Neurological Surgery, UCSF
2014 Young Investigator Award, American Epilepsy Society (AES) Annual Meeting, Seattle, WA
2013 Hanbery Award for Best Paper, San Francisco Neurological Society (SFNS), Napa, CA
2011 Travel Award, Congress of Neurological Surgeons (CNS), Washington, DC
2010 MD/PhD Alumni Award, Yale University
2009 Research Conference Travel Award, NINDS, Washington, DC
2008-09 National Italian American Foundation Academic Scholarship
2008 Educational Stipend, International Society for Magnetic Resonance in Medicine (ISMRM)
2007-10 NRSA for Individual Predoctoral MD/PhD Fellows (F30), NIH (NS059074)
2003 Frank J. O'Hara Award for Top Ranked Graduate by G.P.A., University of Scranton
2003 Excellence in Neuroscience Award, University of Scranton

Extramural Service and Scientific Review

2024 NIH Study Section, BRAIN Initiative Special Emphasis Panel, ZNS1 SRB-E (10), NINDS
2022- Board of Directors, North Amer Neuromodulation Soc (NANS)
2022 NIH Study Section, NST-1, NINDS
2022 NIH Study Section, CTSA Collaborative Innovation Special Emphasis Panel, ZTR1 CI-4 (01)
2022-27 Member, Editorial Board, Journal of Neurosurgery
2022-24 Chair, Scientific Program Com, Amer Soc for Stereotactic Functional Neurosurgery (ASSFN)
2021-24 Chair, Surgical Therapies Commission, Intl League Against Epilepsy (ILAE)
2020-22 Member, Research Recognition Awards Committee, American Epilepsy Society (AES)
2020- Board of Directors, Amer Soc for Stereotactic and Functional Neurosurgery (ASSFN)
2020- Membership Committee, Amer Soc for Stereotactic and Functional Neurosurgery (ASSFN)
2020- Bylaws Committee, Amer Soc for Stereotactic and Functional Neurosurgery (ASSFN)
2020 NIH Study Section, BRAIN Initiative Special Emphasis Panel, ZNS1 SRB-C (07), NINDS
2020 Citizens United for Research in Epilepsy (CURE), Grant Application Review
2019- Contributing Editor, Editorial Board, Epilepsy Currents
2019-25 Member, Editorial Board, Epilepsy & Behavior
2019- Member, Scientific Program Committee, North Amer Neuromodulation Soc (NANS)
2019 American Association of Neurological Surgeons (AANS), Grant Application Review
2018-20 Mentorship Committee, Amer Soc for Stereotactic and Functional Neurosurgery (ASSFN)
2018 American Epilepsy Society (AES), Post-Doctoral Research Grant Application Review
2017-21 Chair, Evidence-Based Epilepsy Surgery Task Force, Intl League Against Epilepsy (ILAE)
2017-18 NIH Study Section, BRAIN Initiative Special Emphasis Panel, ZNS1 SRB-E (10)
2016- Member, Abstract Committee, North Amer Neuromodulation Soc (NANS)
2016-21 Self-Assessment in Neurosurgery Committee, Congress of Neurological Surgeons (CNS)
2016-17 Research Coordinator, Resident/Fellows Board, North Amer Neuromodulation Soc (NANS)

C. Contributions to Science

1) Magnetic resonance imaging (MRI) of arousal network connectivity alterations in epilepsy patients

At Vanderbilt, I began the Brain Imaging and Electrophysiology Network (BIEN) laboratory after starting my first faculty position in 2017. Our lab uses functional MRI (fMRI) and diffusion weighted imaging (DWI) as well as intracranial electroencephography (iEEG) to study brain network disturbances in epilepsy patients. This work was initially supported by an NIH K99/R00 grant, mentored by Vicky Morgan and John Gore, and by the American Epilepsy Society and Epilepsy Foundation, and it is currently supported by NIH R01 awards as PI and co-I. A recent focus of mine has been to characterize perturbations of subcortical-cortical networks important for arousal and vigilance using MRI, and relate these network alterations to neurocognitive factors and disease parameters. We have described both functional (***a***) and structural (***b***) connectivity abnormalities in brainstem reticular formation that appear to be associated with certain neurocognitive deficits in temporal lobe epilepsy patients. In some cases, network connectivity patterns in both brainstem and thalamic arousal pathways may improve towards control values after seizures are reduced with successful epilepsy surgery (***c***).. In one recent study, we

use advanced network analysis and null modelling to demonstrate that nucleus basalis of Meynert is one of the most altered but underappreciated nodes in temporal lobe epilepsy (***d***).

***a*) Englot DJ**, D'Haese PF, Konrad PE, Jacobs ML, Gore JC, Abou-Khalil BW, Morgan VL (2017) Functional connectivity disturbances of the ascending reticular activating system in temporal lobe epilepsy. J Neurol Neurosurg Psychiatry 88(11):925-932. PMC5634927.

***b*) Englot DJ**, Gonzalez HJF, […] Landman BA, Morgan VL (2018) Relating structural and functional brainstem connectivity to disease measures in epilepsy. Neurology 91(1):e67-e77. PMC6091881.

***c*)** González HJF, Chakravorti S, Goodale SE, Gupta K, Claassen DO, Dawant VM, Morgan VL, **Englot DJ** (2019) Thalamic arousal network disturbances in temporal lobe epilepsy and improvement after surgery. J Neurol Neurosurg Psychiatry 90(10):1109-1116. PMC6744309.

d) González HFJ, Narasimhan S, […], Chang C, Morgan VL, Rubinov M, **Englot DJ** (2021) Role of the nucleus basalis as a key network node in temporal lobe epilepsy. Neurology 96(9):e1334-e1346. PMC8055321.

2) Human intracranial EEG (iEEG) to study epileptogenic network connectivity and cortical sequalae

I have led studies using various iEEG analysis techniques to better understand seizure networks in focal epilepsy patients, and evaluate downstream effects on the neocortex. In a project mentored by Hal Blumenfeld at Yale University, we used subdural grid electrodes to evaluate neocortical rhythms associated loss of consciousness during various seizure types in temporal lobe epilepsy patients (***a***). In my own lab at Vanderbilt, we have performed studies using stereo-EEG (SEEG) in focal epilepsy patients, using functional connectivity network analyses to define epileptogenic networks from brief resting-state recordings, and without requiring seizure activity (***b-d***). Specifically, our group have also reported altered directed (effective) connectivity patterns in epileptogenic networks that may help predict seizure onset zones with favorable accuracy (***b***). We also studied the relationship between SEEG connectivity metrics and key potential confounders, such as antiseizure medications and recording state (***c***), as a better understanding of these measures is critical for accurate interpretation of connectivity studies. In the Interictal Suppression Hypothesis we recently proposed that increased inward (but not outward) directed connectivity in epileptogenic regions at rest may reflect inhibitory input to help prevent seizure initiation/propagation.

***a*) Englot DJ**, Yang L, Hamid H, […], Schevon C, Zaveri HP, Blumenfeld H (2010) Impaired consciousness in temporal lobe seizures: role of cortical activity. Brain 133(12):3764-3777. PMC2995886.

***b*)** Narasimhan S, Kundassery KB, Gupta K, […], Morgan VL, Dawant BM, González HJF, **Englot DJ** (2020) Seizure onset regions demonstrate high inward directed connectivity during resting-state: A SEEG study in focal epilepsy. Epilepsia 61(11):2534-2544. PMC7899016.

***c*)** Paulo DL, Wills KE, Johnson GW, […], Williams Roberson S, Narasimhan S, **Englot DJ** (2022) SEEG functional connectivity measures to identify epileptogenic zones: Stability, medication influence, and recording condition. Neurology 98(20):e2060-e2072. PMC9162047.

***d*)** Johnson GW, Doss DJ, […],Wallace MT, **Englot DJ** (2023) The Interictal Suppression Hypothesis in focal epilepsy: Network-level supporting evidence. Brain 146(7):2828-2845. PMC10316780.

3) Magnetoencephalography (MEG) to study brain connectivity and aid localization in focal epilepsy

As a post-doctoral researcher and neurosurgery resident at the University of California, San Francisco (UCSF), I performed studies using MEG to evaluate network connectivity and improve localization of the epileptogenic zone, under the mentorship of Sri Nagarajan and Eddie Chang. First, we examined the long-term effects of consciousness-impairing seizures on brain connectivity using MEG source localization (***a***). We found that recurrent consciousness-impairing seizures in TLE, such as those studied in the aforementioned iEEG investigations (#2, above), are associated with long-term reduction of frontoparietal neocortical functional connectivity. Connectivity impairments appear to be quantitatively related to seizure frequency and disease duration, supporting the clinical relevance of our finding. In various projects, we used MEG to determine which patterns of focal connectivity (***a***), interictal spike activity (***b***), and large amplitude slow activity (***c***) may help localize brain regions producing seizures to facilitate epilepsy surgery planning and outcome prediction. These MEG studies were supported by an NIH F32 training grant. I have also contributed to this field through workshops at national meetings and written commentary on MEG literature (e.g., ***d***).

***a*) Englot DJ**, Hinkley LB, Kort NS, […], Chang EF, Kirsch HE, Nagarajan SS (2015) Global and regional functional connectivity maps of neural oscillations in focal epilepsy. Brain 138:2249-2262. PMC4840946.

***b*) Englot DJ**, Nagarajan SS, Imber BS, Raygor KP, Honma SM, Mizuiri D, Mantle M, Knowlton RC, Kirsch HE, Chang EF (2015) Epileptogenic zone localization using magnetoencephalography predicts seizure freedom in epilepsy surgery. Epilepsia 56(6):949-958. PMC4457690.

***c*) Englot DJ**, Nagarajan SS, Wang DD, Rolston JD, Mizuiri D, Honma SM, Mantle M, Tarapore PE, Knowlton RC, Chang EF, Kirsch HE (2016) The sensitivity and significance of lateralized interictal slow activity on magnetoencephalography in focal epilepsy. Epilepsy Res 121:21-28. PMC4769925.

***d*) Englot DJ** (2019) Addressing a deep problem with magnetoencephalography. Epilepsy Curr 19(5):289-290. PMC6864576.

4) Animal electrophysiology and MRI studies evaluating subcortical network disruption in epilepsy

During my Ph.D. training in Hal Blumenfeld's lab at Yale University, I studied brain network activity during seizures in rodents using electrophysiology, fMRI, laser Doppler flowmetry, and behavioral paradigms. We developed novel rat models of ictal neocortical slow activity, seeking to explain how certain seizures in temporal lobe epilepsy lead to loss of consciousness through transient brain network alterations. We noted that limbic seizures lead to depression of neocortical activity, characterized by reduced neuronal firing, decreased blood flow, diminished fMRI signals, and impaired behavioral responses (***a***). We also found evidence that the negative neocortical and behavioral effects of seizures involve subcortical structures important for arousal, and that preventing seizure spread to these subcortical regions could also prevent neocortical inhibition and behavioral arrest (***b***). These subcortical arousal structures included regions of the thalamus and basal forebrain (***b)***, as well as the brainstem ascending reticular activating system (***c***). The work was funded in part by an NIH F30 training grant. Overall, these finding advanced our understanding of how certain seizures lead to loss of consciousness in temporal lobe epilepsy, and raised important questions regarding possible long-term effects of subcortical network perturbations on behavior and cognition in epilepsy (see ***d***, review).

***a*) Englot DJ,** Mishra AM, Mansuripur PK, Herman P, Hyder F, Blumenfeld H (2008) Remote effects of focal hippocampal seizures on the rat neocortex. J Neurosci 28(36):9066-9081. PMC2590649.

***b*) Englot DJ,** Modi B, Mishra AM, DeSalvo M, Hyder F, Blumenfeld H (2009) Cortical deactivation induced by subcortical network dysfunction in limbic seizures. J Neurosci 29(14):13006-13018. PMC2778759.

***c*)** Motelow JE, Li W, Zhan Q, Mishra AM, Sachdev RNS, Liu G, Gummadavelli A, Zayyad Z, Lee HS, Chu V, Andrews JP, **Englot DJ**, Herman P, Sanganahalli BG, Hyder F, Blumenfeld H (2015) Decreased subcortical cholinergic arousal in focal seizures. Neuron 85(3):561-572. PMC4319118.

***d*) Englot DJ**, Blumenfeld H (2009) Consciousness and epilepsy: why are complex-partial seizures complex? Prog Brain Res 177:147-170. PMC2901990.

5) Clinical studies of epilepsy surgery: Case series, database queries, and meta-analyses

I have led several clinical studies in the field of epilepsy surgery. These have included primary case series to evaluate rates of success and factors associated with failure in surgical resection (e.g., ***a-b***). In one retrospective cohort study of 241 patients undergoing resection for temporal lobe epilepsy, we evaluated rates and factors of freedom from consciousness-impairing and -sparing seizure types after surgery (***a***). In another case series of 125 individuals receiving resection for focal neocortical epilepsy, we observed that surgical failures are more often related to incomplete resection rather than an additional distant epileptogenic region(s) (***b***). I have also performed studies of epilepsy surgery trends and underutilization using national databases such as the U.S. Nationwide Inpatient Sample (***c***). Finally, I have helped lead several systematic reviews and meta-analyses examining rates and predictors of surgical outcome in patients with epilepsy (***d***).

***a*) Englot DJ**, Lee AT, […], Garcia PA, Chang EF (2013) Seizure types and frequency in patients who "fail" temporal lobectomy for intractable epilepsy. Neurosurgery 73(5):838-844. PMID 23892416.

***b*) Englot DJ**, Raygor KP, Molinaro AM, Garcia PA, Knowlton RC, Auguste KI, Chang EF (2014) Factors associated with failed focal neocortical epilepsy surgery. Neurosurgery 75(6):648-656. PMC4393951.

c) Englot DJ, Ouyang D, Garcia PA, Chang EF (2012) Epilepsy surgery trends in the United States, 1990-2008. Neurology 78(16):1200-1206. PMC3324320.

d*)** Touma L, Dansereau B, Chan AY, […], Wong-Kisiel LC, **Englot DJ, Keezer MR* (2022) Neurostimulation in people with drug-resistant epilepsy: Systematic review and meta-analysis from the ILAE Surgical Therapies Commission. Epilepsia 63(6):1314-1329. PMID 35352349.

List of Publications in PubMed: http://www.ncbi.nlm.nih.gov/pubmed/?term=englot+d

Google Scholar Metrics: Citations 8691, h-index 54, i10-index 101 (January 2024)