

BIOGRAPHICAL SKETCH

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NAME: Lisa D Nickerson, Ph.D.

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

POSITION TITLE: Assistant Professor of Psychiatry, Harvard Medical School
Director, Applied Neuroimaging Statistics Lab

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
Purdue University, Indianapolis, IN	B.S.	05/1991	Physics
University of Texas Health Science Center, San Antonio, TX	Ph.D.	05/2001	Physics/Positron Emission Tomography
Harvard Medical School, McLean Hospital	Fellow	06/2001	fMRI Imaging
NIDA T32, Behavioral Psychopharmacology Research Lab, McLean Hospital	Fellow	03/2006	Addiction, Imaging Statistics
Centre for fMRI of the Brain, Oxford University	Visiting	03/2010	Multivariate fMRI

A. Personal Statement

Since joining McLean Hospital, I have worked to become an expert in functional magnetic resonance imaging (fMRI) study design and data analysis. I have over seven years of training under the auspices of NIDA, via T32 and K25 awards, for both imaging statistics and substance use disorders. Through both of these awards, I have had extensive imaging statistics training through coursework, workshops, research projects, and as a visiting scientist at the Oxford Centre for Functional MRI of the Brain (FMRIB). At FMRIB, I worked with Drs. Stephen Smith and Christian Beckmann, pioneers in fMRI data analysis methods and both consultants to the current application, on data-driven statistical methods for the analysis of large-scale brain network functional connectivity. Up until 2013, my research efforts focused on providing statistical analysis support for PIs at McLean Hospital. Since 2013, I have developed my own research program, starting the Applied Neuroimaging Statistics Lab to develop new statistical methods for fMRI and to apply state-of-the-art analysis methods such as multi-modal data fusion to investigate problems of addiction and psychiatric illness. My current research involves advancements in statistical methods for combining large-scale multi-site imaging data, and developing new brain network activation and connectivity analysis techniques and data fusion to investigate the links between brain structure and function in individuals with substance use disorders. My other recent work leverages open access neuroimaging data from the Human Connectome Project (HCP) to develop new statistical methods and to investigate sex differences in the effects of alcohol use disorder (AUD) on brain networks implicated in emotion processing and social cognition. I am also a Biostatistics Consultant for the Harvard Catalyst, providing consultations and expertise on grant applications, manuscripts, and study design and data analysis to researchers throughout the Harvard academic medical and hospital community. I also provide statistical expertise to numerous PIs as a co-investigator on their NIH-funded research studies. A selection of relevant publications is:

1. **Nickerson LD**, Smith SM, Ongur D, Beckmann CF. Using dual regression to investigate network shape and amplitude in functional connectivity analyses. *Frontiers in Neuroscience*. 2017; 11(115):1-18. PMID: 28348512.
2. **Nickerson LD**. Replication of Resting State-Task Network Correspondence and Novel Findings on Brain Network Activation During Task fMRI in the Human Connectome Project Study. *Scientific Reports* 2018; 8:17543.

3. Hu G, Zhang Q, Waters AB, Li H, Zhang C, Wu J, Cong F, **Nickerson LD**. Tensor clustering on outer-product of coefficient and component matrices of independent component analysis for reliable functional magnetic resonance imaging decomposition. *J Neuroscience Methods*, 2019; 325:108359.
4. Li H, Gruber S, Smith SM, Lukas SE, Silveri MM, Hill KP, Killgore WD, **Nickerson LD**. Combining Multi-Site/Study MRI Data: A Novel Linked-ICA Denoising Method for Removing Scanner and Site Variability from Multi-Modal MRI Data. *NeuroImage*, 2020; 208:116388.

B. Positions and Honors

Positions and Employment

1993–2001	Research Stipend Awardee, Radiological Sciences, University of Texas Health Science Center, San Antonio, TX
2001–2003	Research Fellow, Brain Imaging Center, McLean Hospital, Belmont, MA
	Instructor in Psychiatry, Harvard Medical School, Boston, MA
2003–present	Assistant Physicist, Brain Imaging Center and Behavioral Psychopharmacology Research Lab, McLean Hospital
2015–present	Assistant Professor of Psychiatry, Harvard Medical School, Boston, MA
2015–present	Associate Biophysicist, McLean Hospital, Belmont, MA
2015–present	Director, Applied Neuroimaging Statistics Laboratory, McLean Hospital, Belmont, MA

Other Experience and Professional Memberships

2005–2008	Coordinator of McLean Hospital Neuroscience Seminar Series
2010	Tutor, FSL Course, Heidelberg, Germany
2012,2015	Teaching Faculty, MIT–Harvard Health Sciences Tech. Program, fMRI Course HST.583
2012–present	Teaching Faculty, MGH Martinos Center, Functional Connectivity Course
2015–present	Team Leader, Communications Committee, Organization for Human Brain Mapping
2019	Study Section, Neurotoxicology and Alcohol, NIH

Editorial Activities

Associate Editor:	<i>Frontiers in Physics: Biomedical Physics</i> , 2016–2019
Review Editor:	<i>Frontiers in Physics: Interdisciplinary Physics</i>
Reviewer:	<i>JAMA Psychiatry (Archives of General Psychiatry)</i> , <i>NeuroImage</i> , <i>NeuroImage: Clinical</i> , <i>Human Brain Mapping</i> , <i>Drug and Alcohol Dependence</i> , <i>American Journal on Addictions</i> , <i>Brain Connectivity</i> , <i>Bipolar Disorder</i> , <i>Psychiatry Research: Neuroimaging</i> , <i>Neuropsychobiology</i> , <i>Annals of Nuclear Medicine</i>

Memberships

2001–2011	International Society for Magnetic Resonance in Medicine (member/reviewer)
2001–present	Organization for Human Brain Mapping (member/reviewer/Communications Committee)
2014–2016	Attendee/poster presenter at American College of Neuropsychopharmacology (ANCP)

Honors

2001	Honorable Mention, Young Investigator Competition, Society of Nuclear Medicine
2002–2006	NIH Student Loan Repayment Award
2003–2005	NIDA T32 Research Fellow
2005–2010	NIDA K25 Mentored Career Development Award
2008	Taplin Endowment, Research Equipment Award for computing cluster
2012	O’Keefe Family Junior Investigator Award for Excellence in Imaging
2013	Chair, Morning Workshop, 19th Annual Meeting of the Organization for Human Brain Mapping: “Neurotransmitter Function and Intrinsic Brain Functional Connectivity: Studies of GABAergic Inhibitory Neurotransmitter Actions”
2014	Organizer and Speaker, Educational Course, 20th Annual Meeting of the Organization for Human Brain Mapping: “A New Paradigm for Studying Drug Effects: Calibrated fMRI and Resting State Connectivity
2020	Speaker, Symposium on Replicability and Reproducibility for Machine Learning: Applications in Brain Mapping, 26th Annual Meeting of the Organization for Human Brain Mapping: Reliable and Reproducible Brain Network Estimation

C. Contributions to Science

1. Statistical Methods for Neuroimaging: As described above, a consistent theme of my research has been investigating and developing new statistical methods for the analysis of complex brain imaging data in addiction and psychiatry. Most of my efforts have been devoted to investigating and applying sophisticated multivariate statistical methods for MRI data analysis. As mentioned in my Personal Statement, I worked in Oxford UK with Drs. Smith and Beckmann, two pioneers of multivariate methods including independent component analysis (ICA)-based methods for studying brain network connectivity for nearly a year (see also Fillipini et al., 2012). I have also done extensive work in parametric and non-parametric inference methods for fMRI data analysis to improve standard statistical methods for inference on brain maps. We have recently used a state-of-the-art data fusion approach, called linked ICA, to investigate alterations in brain structure and function associated with chronic heavy marijuana use. Key to the success of the endeavor, which combines data from seven different marijuana studies, was the development of a new multivariate statistical method for “denoising” study-specific and scanner effects from multi-site/study MRI data to facilitate combining these data to create a single large dataset. The manuscript describing this approach was recently published in *Neuroimage* (#4 above). I also proposed a new method for investigating the psychophysiological interactions (PPIs) between large-scale brain circuits during task performance. A manuscript describing this innovative new method to probe brain circuits during task performance is in preparation. My NIAAA R21 utilized some of these same techniques to investigate sex differences in the effects of alcohol use disorder using state-of-the-art imaging data collected for the Washington University Human Connectome Project (HCP).
 - a. Li H, **Nickerson LD** (co-first author), Xiong J, Zou Q, Fan Y, Ma Y, Shi T, Ge J, Gao JH. A high performance 3D cluster-based test of unsmoothed fMRI data. *Neuroimage*. 2014; 98:537-46. PubMed PMID: 24836011.
 - b. Li H, **Nickerson LD**, Zhao X, Nichols TE, Gao JH. A voxelation-corrected non-stationary 3D cluster-size test based on random field theory. *Neuroimage*. 2015; 118:676-82. PubMed PMID: 26067343.
 - c. Li H, **Nickerson LD**, Nichols TE, Gao JH. Comparison of a non-stationary voxelation-corrected cluster-size test with TFCE for group-level MRI inference. *Human Brain Mapping*. 2017; 38:1269-1280. PubMed PMID: 27785843.
2. Neurocircuitry of Addiction: I have had a long-standing passion for addiction research that began with my training on a NIDA T32 and NIDA K25 to study the effects of marijuana on brain function. I have published and co-authored research on aspects of alcohol, marijuana, and nicotine, and other addiction-related problems. I have a long-standing collaboration with a lead nicotine investigator in our center, Dr. Amy Janes, that began with the application of independent component analysis to fMRI data to study the effects of nicotine dependence on brain circuitry. Since that publication, we have co-authored several other publications on nicotine dependence (see also other published work). Our nicotine studies have converged to medial prefrontal cortex and insula as being key regions involved in nicotine addiction and cue reactivity. I have also developed a strong collaboration with Dr. Marisa Silveri and her team, Dr. Sneider and Dr. Cohen-Gilbert, to study both alcohol and cannabis use disorders. Our recently published findings show that marijuana abuse in emerging adults leads to alterations in brain structure, and that binge drinking in college students affects inhibitory processing in the context of emotional distractors.
 - a. **Nickerson LD**, Ravichandran C, Lundahl LH, Rodolico J, Dunlap S, Trksak GH, Lukas SE. Cue reactivity in cannabis-dependent adolescents. *Psychol Addict Behav*. 2011; 25(1):168-73. PubMed PMID: 21142334; PubMed Central PMCID: PMC3066287.
 - b. Mashhoon, Y, Sava S, Sneider JT, **Nickerson LD**, Silveri MM. Cortical thinness and volume differences associated with marijuana abuse in emerging adults. *Drug Alcohol Depend*. 2015; 155:275-83. PubMed PMID: 26249265; PubMed Central PMCID: PMC4581973.
 - c. Cohen-Gilbert JE, **Nickerson LD**, Sneider JT, Oot EN, Seraikas AM, Rohan ML, Silveri MM. College binge drinking associated with decreased frontal activation to negative emotional distractors during inhibitory control. *Frontiers Psychology*, 2017; 8:1650
 - d. Janes AC, **Nickerson LD** (co-first author), Frederick Bde B, Kaufman MJ. Prefrontal and limbic resting state brain network functional connectivity differs between nicotine-dependent smokers and non-smoking controls. *Drug Alcohol Depend*. 2012; 125(3):252-9. PubMed PMID: 22459914.

3. **Pharmacologic MRI & Imaging Methods:** I drove efforts to bring novel new acquisition techniques and analysis methods for pharmacologic MRI to investigate the acute effects of drugs to our Imaging Center. These efforts have resulted in numerous collaborations and funding. I have worked with PIs in our center to investigate physiological contributions to resting state fMRI signals and to use quantitative MRI approaches to investigate brain network function that obviates some of the problems associated with using BOLD fMRI for acute drug challenges. My previous R21 (DA032257), a high-risk CEBRA grant, was focused on using perfusion MRI and calibrated BOLD MRI to study the combined acute drug effects of alcohol and nicotine on brain circuitry. Our preliminary findings from the CEBRA showed that transdermal nicotine decreases global cerebral blood flow, which is a significant confound to measuring BOLD signal changes associated with nicotine's effects brain activity, and that for several brain circuits, nicotine and alcohol interact during co-use, with alcohol causing a huge increase in CBF in prefrontal regions and nicotine diminishing alcohol's effects to some extent. The CEBRA was a pilot study to establish quantitative fMRI methods for our studies of drug dependence and provided key pilot results for the investigators on the CEBRA to obtain further funding, including my CEBRA and an R01 held by one of the CEBRA collaborators, Dr. Blaise Frederick. I also presented these findings at the 2014 Annual Meeting for the Organization for Human Brain Mapping in a course that I organized, that also included international leaders in pharmacologic MRI (<https://www.humanbrainmapping.org/i4a/pages/index.cfm?pageID=3622>, "A New Paradigm for Studying Drug Effects: Calibrated fMRI and Resting State Connectivity) to communicate these and related issues to the scientific community. This course led to a publication on CEBRA-related methods with leaders in the field of pharmacologic MRI.
- Frederick Bd, Lindsey KP, **Nickerson LD**, Ryan ET, Lukas SE. An MR-compatible device for delivering smoked marijuana during functional imaging. *Pharmacol Biochem Behav.* 2007; 87(1):81-9. PubMed PMID: 17521714; PubMed Central PMCID: PMC2570055.
 - Tong Y, Hocke LM, **Nickerson LD**, Licata SC, Lindsey KP, Frederick Bd. Evaluating the effects of systemic low frequency oscillations measured in the periphery on the independent component analysis results of resting state networks. *Neuroimage.* 2013; 76:202-15. PubMed PMID: 23523805; PubMed Central PMCID: PMC3652630.
 - Licata SC, **Nickerson LD**, Lowen SB, Trksak, GH, Maclean RR, Lukas SE. The hypnotic zolpidem increases the synchrony of BOLD signal fluctuations in widespread brain networks during a resting paradigm. *Neuroimage* 2013; 70:211-212.
 - Khalili-Mahani N, Rombouts SA, van Osch MJ, Duff EP, Carbonell F, **Nickerson LD**, Becerra L, Dahan A, Evans AC, Soucy JP, Wise R, Zijdenbos AP, van Gerven JM. Biomarkers, designs, and interpretations of resting-state fMRI in translational pharmacological research: A review of state-of-the-art, challenges, and opportunities for studying brain chemistry. *Human Brain Mapping.* 2017; 38(4):2276-2325.

A link to my published work can be found at: <https://www.ncbi.nlm.nih.gov/pubmed/?term=nickerson+ld>.

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

Ongoing

Sub-Contract	Nickerson (Subaward PI)	05/01/19-04/30/20
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President and Fellows of Harvard College and NIH

The Harvard Catalyst aims to advance human health by supporting and innovating clinical and translational science and training the next generation of researchers.

R01NS097512-04	Frederick (PI)	09/01/16-05/31/20
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Mechanisms of Cerebrovascular Reactivity in Health and Disease

This project aims to quantify methods for measuring the health of brain blood vessels to understand the mechanisms underlying vascular dysfunction in individuals with intracranial atherosclerotic stenosis.

Role: Co-Investigator

W81XWH-15-2-0090; Sub-award# 67777771	Stein, UCSD (PI)	09/30/15-03/31/20
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Enhancing fear extinction via Angiotensin Type 1 Receptor inhibition: a randomized controlled trial in posttraumatic stress disorder

The overall study is to test, in a double-blind, placebo-controlled fashion, whether losartan, an angiotensin receptor antagonist, will diminish PTSD symptoms in a multi-site study of civilians and soldiers with PTSD. The following planned analyses will be performed by the Ressler co-I subcontract: 1) Exploratory discovery GWAS and copy number variant (CNV) analyses, 2) Replication analyses from Dr. Ressler's Civilian study highly traumatized civilians with and without PTSD, examining the effects of Angiotensin Converting Enzyme Polymorphisms on PTSD and 3) examining the effects of Angiotensin Receptor Polymorphisms on PTSD.
Role: Co-Investigator

221AD302 Forester (PI) 11/20/15-11/19/22

A Phase 3 Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of Aducanumab (BIIB037) in Subjects with Early Alzheimer's Disease.

The goal is to study the efficacy and safety of a monoclonal antibody, administered by a monthly infusion, compared with placebo for the treatment of mild Alzheimer's Disease and mild neurocognitive impairment.

Role: Co-Investigator

R01MH11927 Kaufman (PI) 04/01/20-01/31/2025

Multimodal approaches to neurobiology of traumatic dissociation

This study will examine behavioral and biological correlates of dissociation across imaging, physiology, and digital assessments. Results from this proposal will inform how to identify those at risk for these debilitating symptoms, potential brain regions to target for treatment, and may support a new standard of clinical care for PTSD with dissociation

Completed Research Support

R01 MH109687 Hall (PI) 03/17/16-01/31/21

Neurobiological Markers as Predictors of Later Functional Outcome in First Episode Psychosis

This project aims to stratify FEP patients into more homogeneous subgroups based on patients' unique neurobiological profiles and relate these profiles to later functional outcome.

Role: Co-Investigator

R21 AA024565 Nickerson (PI) 08/01/16-07/31/19 [NCE]

Sex Differences in the Effects of Alcohol Use Disorder on Brain Circuitry using Existing Data.

This project aims to conduct secondary analyses of existing data collected for the Human Connectome Project, an NIH-funded initiative to comprehensively map human brain circuits and their relationships to behavior in a large population of healthy adults, to investigate sex differences in brain circuitry in individuals with alcohol abuse and dependence.

R21 AG051970 Jain (PI) 04/01/17-01/31/19

Mindfulness and Guided Imagery for Depressed Family Caregivers of Patients with Alzheimer's Disease and Related Dementias: Clinical Outcomes and Neural Mechanisms

This project aims to understand whether a short-term meditation therapy may be helpful to treat depression in family caregivers of dementia patients and identify structural and functional brain changes that correlate with improvements.

Role: Co-Investigator

R01 DA037265 Nickerson (PI) 07/15/14-12/31/18 [NCE]

Multi-Modal MRI Data Fusion to Assess Neurobiological Effects of Marijuana Use

This project aims to combine existing multi-modal MRI data from six different imaging studies using a multivariate data fusion technique to investigate the neurobiology of marijuana use. Machine learning methods will be combined with data fusion to identify patterns of brain structure and function that relate to heavy chronic marijuana use.

Role: PI

R01 AA022493

Silveri (PI)

09/05/14-05/31/19

Consequences of Adolescent Alcohol Use on Brain Development

This project aims to use fMRI, EEG, and behavioral measurements to investigate alcohol use on adolescent brain development.

Role: Co-Investigator

R21 MH112956

Kaufman (PI)

04/01/17-01/31/19

Neurobiology of Traumatic Dissociation in a Transdiagnostic Study of Women with Childhood Maltreatment

This project aims to examine behavioral and brain activity changes related to traumatic dissociation to identify those at risk for these debilitating symptoms and potential brain regions to target for treatment.

Role: Co-Investigator