

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.

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NAME Holtzheimer III, Paul Edgar		POSITION TITLE	
eRA COMMONS USER NAME (credential, e.g., agency login)		Associate Professor	
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	MM/YY	FIELD OF STUDY
Pacific Lutheran University, Tacoma, WA	BS	1990-1995	Biology
Pacific Lutheran University, Tacoma, WA	BA	1990-1995	Psychology/Philosophy
Dartmouth Medical School, Hanover, NH	MD	1995-1999	Medicine
Emory University, Atlanta, GA	MS	2005-2008	Clinical Research

A. Personal Statement: I am a board-certified psychiatrist with >15 years' clinical neuroscience research experience and training including a Master's of Science in Clinical Research. I currently direct the Mood Disorders Service at the Geisel School of Medicine at Dartmouth, which includes the Mood Disorders Research Clinic. I have expertise in the use of neuroimaging and brain stimulation to study clinical and healthy samples. I have extensive experience in the use of MRI (diffusion tensor imaging, resting state fMRI, task fMRI) to study patients with depression. Additionally, I have >15 years' experience in the use of brain stimulation therapies to treat depression, including ECT, TMS and DBS (as well as clinical trials of pharmacologic agents to treat depression). Given my background in brain imaging and brain stimulation, as well as expertise in developing clinical translational applications of these methods, I am well-positioned to participate in this proposed program and related research projects.

B. Positions and Honors.

POSITIONS

- 1999-2003 Psychiatry Residency, University of Washington, Seattle, WA
- 2002-2003 Chief Resident, Outpatient Psychiatry, Harborview Medical Center, Seattle, WA
- 2003-2004 Senior Research Fellow (Transcranial Magnetic Stimulation), University of Washington, Seattle, WA
- 2003-2004 Acting Instructor, University of Washington, Seattle, WA
- 2004-2011 Assistant Professor of Psychiatry and Behavioral Sciences, Emory University, Atlanta, GA
- 2011-present Staff Physician, White River Junction VAMC, White River Junction, VT
- 2011-present Associate Professor of Psychiatry and Surgery, Director, Mood Disorders Service, Geisel School of Medicine at Dartmouth, Dartmouth-Hitchcock Medical Center, Lebanon, NH

HONORS

- 1994 Arête Society, Pacific Lutheran University
- 1995 *Summa cum laude*, Pacific Lutheran University
- 1998 Alpha Omega Alpha, Dartmouth Medical School
- 1998 AMA-Foundation Rock Sleyster Scholar, Dartmouth Medical School
- 1998 Rolf Syvertsen Fellow, Dartmouth Medical School
- 1999 Dartmouth Medical School, M.D. with honors
- 1999 Dean's Medal, Dartmouth Medical School
- 2001 Outstanding Junior Resident, University of Washington Department of Psychiatry
- 2001 American Psychiatric Association/Glaxo-SmithKline Fellow
- 2002 President, American Psychiatric Association/Glaxo-SmithKline Fellows
- 2003 Award for Academic Excellence, University of Washington Department of Psychiatry
- 2003 Outstanding Resident, University of Washington Department of Psychiatry
- 2003 National Institute of Health Loan Repayment Program Award
- 2005 American Federation for Aging Research Young Investigator Award
- 2005 National Institute of Health Loan Repayment Program Award

2007 American Psychiatric Institute Research and Education Research Colloquium for Junior Investigators
2007 NARSAD Young Investigator Award
2007 ACNP Young Investigator Memorial Travel Award
2009 Fourth Year Psychiatry Residents' Teaching Award, Emory University
2010 Third Year Psychiatry Residents' Teaching Award, Emory University
2011 Member, American College of Psychiatrists

C. Selected peer-reviewed publications (in chronological order from >75).

1. **Holtzheimer PE 3rd**, Roberts DW, Darcey TM: Magnetic resonance imaging versus computed tomography for target localization in functional stereotactic neurosurgery. *Neurosurgery* 1999, 45(2):290-7. PMID: 10449073
2. Limonadi FM, Roberts DW, Darcey TM, **Holtzheimer PE 3rd**, Ip JT: Utilization of impedance measurements in pallidotomy using a monopolar electrode. *Stereotactic and Functional Neurosurgery* 1999, 72(1):3-21. PMID: 10640917
3. **Holtzheimer PE 3rd**, Russo J, Avery DH: A meta-analysis of repetitive transcranial magnetic stimulation in the treatment of depression. *Psychopharmacology Bulletin* 2001, 35(4):149-169. PMID: 12397863
4. Avery DH, **Holtzheimer PE 3rd**, Fawaz W, Russo J, Neumaier J, Dunner DL, Haynor DR, Claypoole KH, Wajdik C, Roy-Byrne PP: A controlled study of repetitive transcranial magnetic stimulation in medication-resistant major depression. *Biological Psychiatry* 2006, 59:187-194. PMID: 16139808
5. Avery DH, **Holtzheimer PE 3rd**, Fawaz W, Russo J, Neumaier J, Dunner DL, Haynor DR, Claypoole KH, Wajdik C, and Roy-Byrne P: Transcranial magnetic stimulation reduces pain in patients with major depression: a sham-controlled study. *Journal of Nervous and Mental Diseases* 2007, 195(5): 378-381. PMID: 17502802
6. Gutman DA, **Holtzheimer PE**, Behrens TEJ, Johansen-Berg H, Mayberg HS: A tractography analysis of two deep brain stimulation white matter targets for depression. *Biological Psychiatry* 2009, 65(4):276-282. PMID: 19013554
7. James GA, Kelley ME, Craddock RC, **Holtzheimer PE**, Dunlop B, Nemeroff CB, Mayberg HS, Hu XP: Exploratory Structural equation modeling of resting-state fMRI: applicability of group models to individual subjects. *Neuroimage* 2009, 45:778-787. PMID: 19162206
8. Herbsman T, Avery D, Holt R, Ramsey D, **Holtzheimer P**, Wajdik C, Hardway F, Haynor D, George M, Nahas Z: More lateral and anterior prefrontal coil location improves rTMS antidepressant response. *Biological Psychiatry* 2009, 66(5):509-15. PMID: 19545855
9. Craddock RC, **Holtzheimer PE 3rd**, Hu X, Mayberg HS: Disease state prediction from resting state functional connectivity. *Magnetic Resonance in Medicine* 2009, 62(6):1619-28. PMID: 19859933
10. George MS, Lisanby SH, Avery D, McDonald WM, Durkalski V, Pavlicova M, Anderson B, Nahas Z, Bulow P, Zarkowski P, **Holtzheimer P**, Schwartz T, Sackeim HA: Daily left prefrontal transcranial magnetic stimulation therapy for major depressive disorder: A sham-controlled randomized trial. *Archives of General Psychiatry* 2010, 67:507-516. PMID: 20439832
11. **Holtzheimer PE 3rd**, McDonald WM, Mufti M, Kelley ME, Quinn S, Corso G, Epstein CM: Accelerated repetitive transcranial magnetic stimulation (aTMS) for treatment-resistant depression. *Depress Anxiety* 2010, 27(10):960-963. PMID: 20734360
12. Ramasubbu R, Masalovich S, Gaxiola I, Peltier S, **Holtzheimer PE**, Heim C, Goodyear B, Macqueen G, Mayberg HS: Differential neural activity and connectivity for processing one's own face: A preliminary report. *Psychiatry Res* 2011, 194(2):130-40. PMID: 21962775
13. Craddock RC, James GA, **Holtzheimer PE**, Hu XP, Mayberg HS: A whole brain fMRI atlas generated via spatially constrained spectral clustering. *Hum Brain Mapp* in press (e-pub available). PMID: 21769991
14. **Holtzheimer PE 3rd**, Kelley ME, Gross RE, Filkowski MM, Garlow SJ, Barrocas A, Wint D, Craighead MC, Kozarsky J, Chismar R, Moreines JL, Mewes K, Riva Posse P, Gutman DA, Mayberg HS: Subcallosal cingulate deep brain stimulation for treatment-resistant unipolar and bipolar depression. *Arch Gen Psychiatry* 2012, e-pub available online. PMID: 22213770
15. Broadway JM, **Holtzheimer PE**, Hilimire MR, Parks NA, DeVylder JE, Mayberg HS, Corballis PM: Frontal theta cordance predicts 6-month antidepressant response to subcallosal cingulate deep brain stimulation for treatment-resistant depression: A pilot study. *Neuropsychopharmacology*, in press, e-pub available online. PMID: 22414813
16. Johnson KA, Baig M, Ramsey D, Lisanby SH, Avery D, McDonald WM, Li X, Bernhardt ER, Haynor DR, **Holtzheimer PE 3rd**, Sackeim HA, George MS, Nahas Z: Prefrontal rTMS for treating depression: Location and intensity results from the OPT-TMS multi-site clinical trial. *Brain Stimul* in press, e-pub available online. PMID: 22465743
17. Riva-Posse P, **Holtzheimer PE**, Garlow SJ, Mayberg HS: Practical Considerations in the Development and Refinement of Subcallosal Cingulate White Matter Deep Brain Stimulation for Treatment Resistant Depression. *World Neurosurg* in press, available online 2012.
18. McGrath CL, Kelley ME, **Holtzheimer PE**, Dunlop BW, Craighead WE, Franco AR, Craddock RC, Mayberg HS: Toward a Neuroimaging Treatment Selection Biomarker for Major Depressive Disorder. *JAMA Psychiatry* in press.

D. Research Support (past three years).

Dartmouth Synergy Grant (Co-PIs: Paul Holtzheimer, MD; Yu-Chien Wu, MD, PhD) ONGOING
Dartmouth College

“High Angular Resolution Diffusion Imaging (HARDI) with novel HYPR image reconstruction”
The goal of the proposed pilot project is to begin development of a novel, fast imaging technique for a high angular resolution diffusion imaging method (HARDI) that can be acquired quickly. To do this, HARDI acquisition will be combined with an advanced approach to rapid image reconstruction (HighLY constrained back PROjection reconstruction (HYPR)). The preliminary data from this project will help justify pursuing external funding to expand this work

R01 MH091100-A1 (PI: Paul Holtzheimer, MD) ONGOING
National Institute of Mental Health

“Identifying Biomarkers for Treatment-Resistant Depression Using Resting-State Functional Connectivity”
This project will investigate the neurobiology of treatment-resistant depression (TRD) using functional magnetic resonance imaging functional connectivity analyses. These findings will increase our understanding of the pathophysiology of TRD and will guide further research including the development of novel interventions for this prevalent and costly disorder.

2009-2011 Sub-contract (PI: Paul Holtzheimer, MD) COMPLETED
UCSF/Greenwall Foundation (PI: Laura Dunn, MD)

“Examining Ethical Issues in Deep Brain Stimulation Research”
Using a number of survey and interview methods, this project will examine ethical issues related to informed consent and decision-making capacity in patients considering participation in clinical trials of deep brain stimulation for treatment-resistant depression.

2007-2011 K23 077869- 02 (PI: Paul Holtzheimer, MD) COMPLETED
National Institute of Mental Health

“Investigating Structural and Functional Brain Abnormalities in Late-Life Depression”
A patient-oriented mentored research project that uses magnetic resonance imaging (structural imaging, diffusion tensor imaging and task-activated functional magnetic resonance imaging) to study structural and functional brain abnormalities in 40 patients with late-life depression and 40 healthy controls.
Role: Principal Investigator

2007-2010 Clinical Neuroscience Research Grant (PI: Helen Mayberg, MD) COMPLETED
Dana Foundation

“Deep Brain Stimulation Clinical Research Program for Treatment-Resistant Depression”
Pilot study of deep brain stimulation of the Brodmann Area 25 white matter as a treatment for treatment-resistant major depression. Study also includes mechanism of action studies including PET imaging, neuroendocrine assays, genetic testing and EEG analyses.
Role: Co-Investigator