OMB No. 0925-0001 and 0925-0002 (Rev. 10/2021 Approved Through 09/30/2024)

BIOGRAPHICAL SKETCH

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NAME: DeLorenzo, Christine

eRA COMMONS USER NAME (credential, e.g., agency login): cd2415

POSITION TITLE: Professor; Director, Center for Understanding Biology Using Imaging Technology

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
Dartmouth College, Hanover, NH	B.A.	1999	Engineering
Dartmouth College, Hanover, NH	M.S.	2001	Biomed. Engineering
Yale University, New Haven, CT	Ph.D.	2007	Biomed. Engineering
Columbia University, New York, NY	Post-doc	2011	Psychiatry

A. Personal Statement

As the Director of the Center for Understanding Biology using Imaging Technology (CUBIT) at Stony Brook, I am responsible for decisions on pilot funding for brain imaging (as part of the Brain Imaging Pilot Program through the PET Core). The Brain Imaging Pilot Program provided 10 pilot awards (4 to women) to investigators interested in using PET for brain imaging studies. It resulted in seven NIH-funded proposals (3 to women). This role, combined with being a chartered member of the Emerging Imaging Technologies in Neuroscience (EITN) study section, provides me with a wealth of experience to draw upon to lead the pilot program. I am excited to leverage my experience to lead Module D2 into innovative solutions for Clinical and Translational Science (CTS). I will work with the Management Committee of the Module and the entire LINCATS team to fulfill the goals of LINCATS, bringing communities, collaborators and scholars together to promote CTS.

In addition, CUBIT provides outreach aiding new investigators in starting brain imaging projects. The Research Concierge position is partially based on this arrangement. This outreach includes preparing applications for internal pilot funding, government and private foundations as well as assistance developing imaging protocols and submission to the Institutional Review Board (IRB). I will use a similar model for training the Research Concierge to aid pilot program awardees.

I have a great deal of experience recruiting participants for translational imaging studies, including vulnerable populations. The studies below involved imaging before and/or after antidepressant treatment.

1. Esterlis I, DellaGioia N, Pietrzak RH, Matuskey D, Nabulsi N, Abdallah C, Yang J, Pittenger C, Sanacora G, Krystal JH, Parsey, RV, Carson RE, **DeLorenzo C**: Ketamine-induced reduction in mGluR5 availability is associated with an antidepressant response: an [^{11}C]ABP688 and PET imaging study in depression, *Molecular Psychiatry*. 23(4):824-832, 2018. (PMC5636649)
2. Ananth M, **DeLorenzo C**, Yang J, Mann JJ, Parsey R: Decreased pretreatment amygdalae serotonin transporter binding in unipolar depression remitters: a prospective PET study, *Journal of Nuclear Medicine* 59(4):665-670. 2018. (PMC5932749)
3. Pillai RLI, Huang C, LaBella A, Zhang M, Yang J, Trivedi M, Weissman M, McGrath P, Fava M, Kurian B, Cooper C, McInnis M, Oquendo MA, Pizzagalli DA, Parsey RV, **DeLorenzo C.** Examining raphe-amygdala structural connectivity as a biological predictor of SSRI response. *J Affect Disord*. 256:8-16, 2019. (PMC6750958)
4. Hill KR, Gardus JD, Bartlett EA, Perlman G, Parsey RV, **DeLorenzo C:** Measuring brain glucose metabolism in order to predict response to antidepressant or placebo: A randomized clinical trial. *Neuroimage: Clin,* 2021 (PMC8551925)

Ongoing Research Support

NIH, R01MH123093 (MPI: DeLorenzo, Parsey) 05/20 – 02/25
A translational study of neuroinflammatory depression: Understanding mechanism and evaluation of a novel pharmacologic intervention
The goal of this study is to understand the role of neuroinflammation in depression. The study involves a human component and a mouse component. The human participants have major depressive disorder and the mice are induced to have "depression-like" symptoms. Preclinical studies are performed by Dr. Tsirka, who is a coinvestigator. The study will examine whether people/rodents with the highest levels of neuroinflammation are the more responsive to anti-inflammatories. Neuroinflammation will be quantified using PET/microPET and the tracer [^{18}F]FEPPA.

NIA, RF1AG064245 (PI: DeLorenzo) 09/19 – 03/24
Assessing cholinergic circuits and spatial memory loss: a translational study of Alzheimer's disease and a model of cognitive decline
Age-related cognitive decline is a growing problem. The cholinergic system has long been implicated in significant cognitive decline such as in Alzheimer's disease. What is unknown is the role of the cholinergic system in this cognitive decline. This comprehensive study utilizes both human participants as well as an animal model of accelerated aging to investigate the contribution of the cholinergic system in age-related cognitive decline. In both humans and mice, we use *in vivo* PET with a novel tracer that labels the cholinergic system, to understand cell specific changes to cholinergic function. Parallel studies using *in vivo* extracellular recordings in the mouse model will allow us to investigate circuit level changes in the basal forebrain cholinergic nuclei to the entorhinal cortex.

NIMH, R01MH114972 (PI: DeLorenzo) 08/18 – 05/23
Role of the metabotropic glutamate receptor subtype 5 in circadian rhythm misalignment and depression: Implications for treatment
In this study, we examine the role of the metabotropic glutamate receptor subtype 5 (mGluR5) in circadian rhythm dysfunction and depression. We will chronotype both healthy controls and those with major depressive disorder (MDD). mGluR5 density will be measures at certain points within the circadian rhythm. The change in circadian rhythms after sleep deprivation therapy is also examined and related to MDD improvement.

Completed Research Support

NYS Department of Economic Development, Faculty Development Program 01/19 – 12/21
Brain Imaging to Improve Diagnosis, Monitoring and Treatment of Depression
The purpose of the Faculty Development Program is to either attract distinguished faculty from throughout the world to New York's academic institutions of higher education; or retain leading researchers already working in academic institutions of higher education in New York. I was awarded this based on my imaging research in depression performed at Stony Brook University.

Alzheimer's Foundation of America (PI: DeLorenzo) 6/18 – 6/21
Imaging Memory Circuits in Health and Alzheimer's Disease in Order to Improve Memory Treatments
The goal of this study is to improve our understanding of how memory works, in both healthy individuals and those with Alzheimer's disease (AD) by studying: (1) the structure and function of cholinergic neurons in health and (2) how these neurons are damaged in AD. In this way, we can develop medications that specifically target the damage and return the neurons to a state of health. To perform this study, we will take advantage of two unique resources: a mouse model in which the cholinergic neurons are "highlighted," allowing us to map them out in high resolution post mortem. And, Positron Emission Tomography imaging which allows us to visualize and quantify the cholinergic system in the living mouse and human brain.

NIMH, R01MH104512 (PI: DeLorenzo) 05/15 – 01/20 (NCE)
Advancing Personalized Antidepressant Treatment Using PET/MRI
The purpose of this study is to understand the mechanism of action of antidepressants (SSRIs) using PET and two MRI sequences – anatomical MRI and Arterial Spin Labeling (ASL, which allows examination of blood flow). The MRI sequences allow for novel quantification of PET images in a way that may obviate the need for arterial blood draws in the future. Study aims include two clinical aims: (1) Determine whether pretreatment metabolic rate of glucose (MRGlu) is correlated with antidepressant-induced changes. (2) Isolate the neurobiological basis of the "Loss" Research Domain Criteria (RDoc). And two technical aims: (3) Validate

noninvasive full quantification of MRGlu using simultaneous estimation (SimE). SimE fully quantifies brain MRGlu without requiring arterial blood analysis. It can instead use information from MRI sequences like ASL. (4) Validate noninvasive estimates of plasma radioactivity from a novel mini PET scanner.

NARSAD Young Investigator Grant, Brain & Behavior Research Foundation (PI:D'Agostino)
The effect of celecoxib on neuroinflammation in MDD 06/17 – 06/19
To investigate neuroinflammation as a potential treatment target for MDD, this pilot study involves conducting [^{18}F]FEPPA PET scans in individuals with MDD before and after celecoxib treatment. We hypothesize that following celecoxib treatment, patients will show a significant reduction in neuroinflammation, which will correlate positively with the reduction in depressive symptoms.
Role: Mentor

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2021- Professor, Departments of Psychiatry and Biomedical Engineering
Stony Brook University, Stony Brook, NY
2021-2016 Associate Professor, Departments of Psychiatry and Biomedical Engineering
Stony Brook University, Stony Brook, NY
2016-2012 Assistant Professor, Departments of Psychiatry and Biomedical Engineering
Stony Brook University, Stony Brook, NY
2012- Director, Center for Understanding Biology using Imaging Technology (CUBIT)
Stony Brook University, Stony Brook, NY
2012- Adjunct Assistant Professor, Psychiatry, Columbia University, New York, NY
2012-2011 Assistant Professor, Psychiatry, Columbia University, New York, NY
2011-2008 Postdoctoral Research Fellow, Psychiatry, Columbia University, New York, NY
2007-2001 Graduate Research Fellow, Biomedical Engineering, Yale University, New Haven, CT
2001-1999 Graduate Research Fellow, Biomedical Engineering, Dartmouth College, Hanover, NH

Other Experience and Professional Memberships

2022- Member, American College of Neuropsychopharmacology (ACNP)
2018- NIH Emerging Imaging Technologies in Neuroscience (EITN), Chartered Member
2012- Associate Editor, Frontiers in Neuropharmacology

Honors

2019 Excellence in Research Award, Department of Biomedical Engineering, Stony Brook University
2019 Senior Research Excellence Award. The purpose of this award is to "recognize and reward excellence among faculty in the various mission areas of the Renaissance School of Medicine."
2014 Chairman's Choice Award, Society of Biological Psychiatry
2007 Robert E. Apfel Graduate Fellowship Award Winner for Creativity in Research and Contributions to the Community, Yale University
2007 Prize Teaching Fellowship Recipient for Outstanding Teaching Performance, Yale University

C. Contributions to Science

1. I have performed inquiries into the glutamatergic system using PET. In the work below, I examine one of the glutamate receptors, the metabotropic glutamate receptor subtype 5 (mGluR5), in MDD. I also examined the effects of ketamine, a novel antidepressant, on mGluR5. This work sheds light on the pathophysiology of depression as well as helps in developing new therapies. Our ketamine studies provided first evidence of the effect of ketamine on mGluR5 using PET in human subjects and suggests that the PET tracer used ([^{11}C]ABP688) is sensitive to ketamine-induced effects.
    a. **DeLorenzo C**, Kumar JSD, Mann JJ, and Parsey RV. *In Vivo* Variation in Metabotropic Glutamate Receptor Subtype 5 Binding Using Positron Emission Tomography and [^{11}C]ABP688. *Journal of Cerebral Blood Flow & Metabolism*, 31(11):2169-80, 2011. (PMC3210337)
    b. **DeLorenzo C**, DellaGioia N, Bloch M, Sanacora G, Nabulsi N, Abdallah C, Yang J, Wen R, Mann, JJ, Krystal JH, Parsey, RV, Carson RE, Esterlis I: *In vivo* ketamine-induced changes in [^{11}C]ABP688 binding to metabotropic glutamate receptors subtype 5, *Biological Psychiatry*, 77(3):266-75, 2015. (PMC4277907)
    c. **DeLorenzo C**, Sovago J, Gardus J, Xu J, Yang J, Behrje R, Kumar JS, Devanand DP, Pelton GH, Mathis CA, Mason NS, Gomez-Mancilla B, Aizenstein H, Mann JJ, Parsey RV: Characterization of

brain mGluR5 binding in a pilot study of late-life major depressive disorder using positron emission tomography and [^{11}C]ABP688, *Translational Psychiatry*, Dec 2015. (PMC5068588)

d. **DeLorenzo C**, Gallezot JD, Gardus J, Yang J, Planeta B, Nabulsi N, Ogden RT, Labaree DC, Huang YH, Mann JJ, Gasparini F, Lin X, Javitch JA, Parsey RV, Carson RE, Esterlis I. *In vivo* variation in same-day estimates of metabotropic glutamate receptor subtype 5 binding using [^{11}C]ABP688 and [^{18}F]FPEB. *Journal of Cerebral Blood Flow & Metabolism*, 37(8):2716-2727, 2017. (PMC5536783)

2. Most studies performed in my lab are in pursuit of advancing our understanding of depression. Knowledge gained from these types of studies can be used to enhance diagnosis and treatment. For the studies below, I have recruited cohorts of depressed patients, carefully characterized their depression and performed PET and MRI imaging to better understand the biology of this disease. These studies indicate our strong commitment to improving the lives of people with depression, and the care taken with this population to allow them to enroll in and complete these complex studies.
    a. Iscan Z, Rakesh G, Rossano S, Yang J, Zhang M, Miller J, Sullivan GM, Sharma P, McClure M, Oquendo MA, Mann JJ, Parsey RV, **DeLorenzo C**: A positron emission tomography study of the serotonergic system in relation to anxiety in depression, *Eur Neuropsychopharmacology,* 27(10):1011-1021, 2017. (PMC5623123)
    b. Delaparte L, Yeh FC, Adams P, Malchow A, Trivedi MH, Oquendo MA, Deckersbach T, Ogden T, Pizzagalli DA, Fava M, Cooper C, McInnis M, Kurian BT, Weissman MM, McGrath PJ, Klein DN, Parsey RV, **DeLorenzo C**. A comparison of structural connectivity in anxious depression versus non-anxious depression. *Journal of Psychiatric Research*, 89:38-47, 2017. (PMC5374003)
    c. Pillai RLI, Malhotra A, Rupert DD, Weschler B, Williams JC, Zhang M, Yang J, Mann JJ, Oquendo MA, Parsey RV, **DeLorenzo C**. Relations between cortical thickness, serotonin 1A receptor binding, and structural connectivity: A multimodal imaging study. *Human Brain Mapping*, 39(2):1043-1055, 2018. (PMC5769701)
    d. Pillai RLI, Bartlett EA, Ananth MR, Zhu C, Yang J, Hajcak G, Parsey RV, **DeLorenzo C**. Examining the underpinnings of loudness dependence of auditory evoked potentials with positron emission tomography. *Neuroimage.* 2020 (PMC7254571)

3. My research goal is to use the most advanced methods to quantify brain images. In pursuit of the goal, I have characterized neuroimages from multiple PET tracers as well as MRI in order to determine the most accurate quantification techniques. For new PET tracers, important decisions must be made about proper PET scan times, time activity curve modeling techniques, the necessity of an arterial input function and existence of a reference region. These issues should be (but often are not) methodically addressed at this early stage of tracer development or we risk the loss of much time, effort and research funds, by performing PET studies with suboptimal quantification strategies. With a background in medical image analysis, I am able to determine the optimal methods for quantification. This includes developing novel algorithms as needed. For example, when performing a study using the ligand [^{11}C]PE2I, which targets the dopamine transporter, I realized that the standard PET to MRI registration technique was suboptimal for this ligand due to its localized binding. To overcome this problem, I developed and implemented an improved, automated PET-MRI registration technique. The quality of this PET-MRI registration technique was so high that JCBFM editors chose a figure from my manuscript of a PET image overlaid on MRI (using this technique) as their cover image for issue in which (a) below is published. For MRI, I have carefully evaluated the reliability of MRI-derived measures including volume and cortical thickness.
    a. **DeLorenzo C**, Kumar JS, Zanderigo F, Mann JJ, and Parsey RV. Modeling considerations for *in vivo* quantification of the dopamine transporter using [(11)C]PE2I and positron emission tomography. Journal of Cerebral Blood Flow & Metabolism, 29(7):1332-45, 2009. (PMC2757108)
    b. Milak MS, **DeLorenzo C**, Zanderigo F, Prabhakaran J, Kumar JS, Majo VJ, Mann JJ, Parsey RV: *In vivo* quantification of human serotonin 1A receptor using ^{11}C-CUMI-101, an agonist PET radiotracer. The Journal of Nuclear Medicine, 29(2):322-38, 2010. (PMC3856257)
    c. Iscan Z, Jin TB, Kendrick A, Szeglin B, Lu H, Trivedi M, Fava M, McGrath PJ, Weissman M, Kurian BT, Adams P, Weyandt S, Toups M, Carmody T, McInnis M, Cusin C, Cooper C, Oquendo M, Parsey RV, **DeLorenzo C**. Test-Retest Reliability of Freesurfer Measurements Within and Between Sites: Effects of Visual Approval Process, Human Brain Mapping, 36(9):3472-85, 2015. (PMC4545736)

d. Bartlett EA, Ananth M, Rossano S, Zhang M, Yang J, Lin SF, Nabulsi N, Huang Y, Zanderigo F, Parsey RV, **DeLorenzo C** Quantification of Positron Emission Tomography Data Using Simultaneous Estimation of the Input Function: Validation with Venous Blood and Replication of Clinical Studies. *Mol Imaging Biol.* Oct;21(5):926-934, 2019. (PMC6555699)

4. I have a great deal of experience in the acquisition and analysis of large *in vivo* datasets. For my doctoral research, I developed an algorithm to update preoperative MRI images to reflect the intraoperative brain, which may deform during surgery. Because this deformation causes a mismatch between the preoperative views of the brain used for surgical planning / guidance and the current state of the brain on the operating table, it is a significant problem. I therefore designed an algorithm using game theory, probability theory, computer vision, and statistical optimization. This algorithm was able to use digital images of the intraoperative brain surface to determine the extent of brain surface deformation, and then propagated that deformation throughout the brain volume by means of a biomechanical model. It was even able to overcome issues related to inaccurate camera calibration by means of game theory (found the Nash equilibrium between updated camera calibration parameters and predicted surface displacement). Since the algorithm only requires a computer and inexpensive digital camera, and uses a multidisciplinary approach, I was awarded Yale University's Robert E. Apfel Fellowship Award for creativity in research and contributions to the community for this work.
    a. **DeLorenzo C**, Papademetris X, Vives KP, Spencer D, Wu K, Duncan JS: Nonrigid 3D Brain Registration Using Intensity/Feature Information, Medical Image Computing and Computer Assisted Intervention (MICCAI), Copenhagen, Denmark, 932-939, 2006.
    b. **DeLorenzo C**, Papademetris X, Staib LH, Vives KP, Spencer DD, Duncan JS: Nonrigid Intraoperative Cortical Surface Tracking Using Game Theory, IEEE 11th International Conference on Computer Vision (ICCV), Rio de Janeiro, Brazil, 1-8, 2007.
    c. **DeLorenzo C**, Papademetris X, Staib LH, Vives KP, Spencer DD, and Duncan JS. Image-Guided Intraoperative Cortical Deformation Recovery Using Game Theory: Application to Neocortical Epilepsy Surgery. IEEE Transactions on Medical Imaging, 29(2):322-38, 2010. (PMC2824434)
    d. **DeLorenzo C**, Papademetris X, Staib LH, Vives KP, Spencer DD, Duncan JS: Volumetric Intraoperative Brain Deformation Compensation: Model Development and Phantom Validation, IEEE Transactions on Medical Imaging, 31(8)1607-19, 2012 (PMC3600363)

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/christine.delorenzo.1/bibliography/41173244/public/?sort=date&direction=descending