OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.

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| NAME: Provenzano, Frank A |
| eRA COMMONS USER NAME (credential, e.g., agency login): PROVENZANO |
| POSITION TITLE: Assistant Professor of Neurological 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) | END DATE MM/YYYY | FIELD OF STUDY |
| Columbia University, New York, NY | BS | 05/2006 | Biomedical Engineering |
| Columbia University, New York, NY | MS | 05/2012 | Biomedical Engineering |
| Columbia University, New York, NY | MPHIL | 05/2015 | Biomedical Engineering |
| Columbia University, New York, NY | PHD | 02/2016 | Biomedical Engineering |

### A. Personal Statement

Functional brain imaging's role in both clinical and research setting is evolving significantly. Specifically, the mapping of functional changes to regions has progressed from novelty to utility. Capitalizing on the availability of multi-site open data for both neurological and psychiatric disorders. I have evaluated and developed techniques to overcome some of the challenges of organizing, harmonization and synthesizing structural neuroimaging data.

To this point, much of my work focuses on new techniques applied frequently acquired from large scale neuroimaging and the applications of those methods to understand pathology as well test the feasibility of applying those methods to clinical data. These techniques are based on previous work, including multi-modal analysis in Alzheimer's disease (Provenzano et al. 2013), as well as the development of tools to examine high-resolution functional imaging in Alzheimer's (Khan et al. 2013) and in interventional clinical trials.

Informed by my experience in biomedical image analysis, neurology, psychiatry and programming, my goals have been to re-examine routine imaging to unearth potentially useful functional metrics and biomarkers using machine learning and improved quality control techniques. This is true especially for diseases where neuroimaging metrics are a part of the clinical diagnostic criteria, such as multiple sclerosis.

I apply this experience with broad applications of research in aspects of neuroimaging, especially where MRIs are "acquired but not fully used", in a large setting using large multi-site studies. Recently, I have led studies that explore Alzheimer's diagnostics and age-prediction (Feng, Lipton et al. 2019) using deep learning MRI on very large scale (10,000+) datasets while robustly examining the regional contributions to these prediction models (Feng, Yang et al. 2018).

1. Feng X, Lipton Z, Yang J, Small S, Provenzano F. Estimating brain age based on a healthy population with deep learning and structural MRI. arXiv:1907.00943 [cs, eess, q-bio]. 2019 July 01;
2. Feng X, Yang J, Lipton Z, Small S, Provenzano F, Disease Neuroimaging Initiative A. Deep Learning on MRI Affirms the Prominence of the Hippocampal Formation in Alzheimer’s Disease Classification. [Preprint]. 2018 October 31; :456277.
3. Khan UA, Liu L, Provenzano FA, Berman DE, Profaci CP, Sloan R, Mayeux R, Duff KE, Small SA. Molecular drivers and cortical spread of lateral entorhinal cortex dysfunction in preclinical Alzheimer's disease. Nat Neurosci. 2014 Feb;17(2):304-11. PubMed PMID: [24362760](http://www.ncbi.nlm.nih.gov/pubmed/24362760/); PubMed Central PMCID: [PMC4044925](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4044925/).
4. Provenzano FA, Muraskin J, Tosto G, Narkhede A, Wasserman BT, Griffith EY, Guzman VA, Meier IB, Zimmerman ME, Brickman AM. White matter hyperintensities and cerebral amyloidosis: necessary and sufficient for clinical expression of Alzheimer disease?. JAMA Neurol. 2013 Apr;70(4):455-61. PubMed PMID: [23420027](http://www.ncbi.nlm.nih.gov/pubmed/23420027/); PubMed Central PMCID: [PMC4124641](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4124641/).

### B. Positions and Honors

Positions and Employment

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| --- | --- |
| 2011 - 2015 | Graduate Research Assistant, Columbia University, New York, NY |
| 2016 - 2017 | Postdoctoral Scientist, College of Physicians and Surgeons, Columbia University, New York, NY |
| 2017 - | Assistant Professor of Neurological Sciences, Taub Institute, Columbia University College of Physicians and Surgeons, Columbia University, New York, NY |

Other Experience and Professional Memberships

Honors

### C. Contribution to Science

1. Prior to graduate school, I helped develop techniques for the automated segmentation of white matter hyperintensities and study how their location and volume relate to Alzheimer's disease risk, aging and cognition. These techniques along with other imaging modalities have helped clarify the potential role of PET amyloid imaging as it relates to disease risk.
   1. Provenzano FA, Muraskin J, Tosto G, Narkhede A, Wasserman BT, Griffith EY, Guzman VA, Meier IB, Zimmerman ME, Brickman AM. White matter hyperintensities and cerebral amyloidosis: necessary and sufficient for clinical expression of Alzheimer disease?. JAMA Neurol. 2013 Apr;70(4):455-61. PubMed PMID: [23420027](http://www.ncbi.nlm.nih.gov/pubmed/23420027/); PubMed Central PMCID: [PMC4124641](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4124641/).
   2. Brickman AM, Meier IB, Korgaonkar MS, Provenzano FA, Grieve SM, Siedlecki KL, Wasserman BT, Williams LM, Zimmerman ME. Testing the white matter retrogenesis hypothesis of cognitive aging. Neurobiol Aging. 2012 Aug;33(8):1699-715. PubMed PMID: [21783280](http://www.ncbi.nlm.nih.gov/pubmed/21783280/); PubMed Central PMCID: [PMC3222729](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3222729/).
2. Interrogate sub-regions of human hippocampus with the highest spatial resolution available for studies of greater than thirty subjects.
   1. Brickman AM, Khan UA, Provenzano FA, Yeung LK, Suzuki W, Schroeter H, Wall M, Sloan RP, Small SA. Enhancing dentate gyrus function with dietary flavanols improves cognition in older adults. Nat Neurosci. 2014 Dec;17(12):1798-803. PubMed PMID: [25344629](http://www.ncbi.nlm.nih.gov/pubmed/25344629/); PubMed Central PMCID: [PMC4940121](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4940121/).
   2. Khan UA, Liu L, Provenzano FA, Berman DE, Profaci CP, Sloan R, Mayeux R, Duff KE, Small SA. Molecular drivers and cortical spread of lateral entorhinal cortex dysfunction in preclinical Alzheimer's disease. Nat Neurosci. 2014 Feb;17(2):304-11. PubMed PMID: [24362760](http://www.ncbi.nlm.nih.gov/pubmed/24362760/); PubMed Central PMCID: [PMC4044925](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4044925/).
3. Was the first to successfully generate functional measurements from unrelated clinically-acquired retrospective contrast-enhanced clinical neuroimaging. This was demonstrated as being more sensitive than volume measurements for certain clinical uses and this method can be applied to millions of MRI scans acquired clinically to generate functional measures.
   1. Feng X, Hamberger MJ, Sigmon HC, Guo J, Small SA, Provenzano FA. Temporal lobe epilepsy lateralization using retrospective cerebral blood volume MRI. Neuroimage Clin. 2018;19:911-917. PubMed PMID: [30003028](http://www.ncbi.nlm.nih.gov/pubmed/30003028/); PubMed Central PMCID: [PMC6039834](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC6039834/).
4. Assembled and tested one of the most diverse collections of images to predict age using a deep learning convolutional neural network in structural MRI as well as generated models in predicting Alzheimer's disease and prodromal Alzheimer's disease.
   1. Feng X, Yang J, Lipton Z, Small S, Provenzano F, Disease Neuroimaging Initiative A. Deep Learning on MRI Affirms the Prominence of the Hippocampal Formation in Alzheimer’s Disease Classification. [Preprint]. 2018 October 31; :456277.
5. I applied and investigated multimodal neuroimaging in individuals at clinical high risk for psychosis (CHR). (Provenzano et al. 2018) This helped elucidate the role of hippocampal pathology both in this high risk group as well as explore potential mechanisms that differentially affect the hippocampus and more specifically the CA1 subregion in risk for and conversion to psychosis.
   1. Provenzano FA, Guo J, Wall MM, Feng X, Sigmon HC, Brucato G, First MB, Rothman DL, Girgis RR, Lieberman JA, Small SA. Hippocampal Pathology in Clinical High-Risk Patients and the Onset of Schizophrenia. Biol Psychiatry. 2020 Feb 1;87(3):234-242. PubMed PMID: [31771861](http://www.ncbi.nlm.nih.gov/pubmed/31771861/).

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

Ongoing Research Support

R01MH113861-01, NIMH

Girgis (PI)

09/01/17-05/31/22

The Neurobiology of Violence in a Psychosis-Risk Cohort

The goal is to determine how to best ask about thoughts of violence, obtain comprehensive assessment of symptom correlates of violent thoughts and actions, and investigate relationships between violent thoughts and brain abnormalities

Role: KP

R01AG060979, NIH

Sloan (PI)

09/01/18-08/31/23

Age-Related Memory disorders: Testing a Dietary Intervention and Neuroinflammatory Mediator

In this application, we propose to test this mechanism in a randomized controlled trial in which healthy older adults receive cocoa flavanols or placebo daily for a 12-week period, with pre- and post-intervention MRIs to assess the function of this brain region and blood draws to measure key inflammatory markers.

Role: KP

Completed Research Support

R61MH112800, NIMH

Small (PI)

07/05/17-06/30/19

Glutamate reducing interventions in schizophrenia

To test the effectiveness of the medication Pomaglumetad in the reduction of psychotic symptoms on prodromal subjects.

Role: KP