OMB No. 0925-0001 and 0925-0002 (Rev. 10/15 Approved Through 10/31/2018)

# BIOGRAPHICAL SKETCH

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NAME: Horga Hernández, Guillermo, M.D., Ph.D.

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

POSITION TITLE: Assistant Professor

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.)*

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| INSTITUTION AND LOCATION | DEGREE  *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
| Universidad Miguel Hernández of Elche, Spain | M.D. | 05/2004 | Medicine and Surgery |
| Hospital Clinic of Barcelona, Barcelona, Spain | Residency | 05/2009 | Psychiatry |
| University of Barcelona, Barcelona, Spain | Ph.D. | 05/2015 | Clinical Neuroscience |
| Columbia University, New York, NY | Fellowship | 06/2012 | Psychiatric Research |

# Personal Statement

Guillermo Horga, MD, PhD, is a Florence Irving Assistant Professor of Psychiatry at Columbia University and the New York State Psychiatric Institute. He is clinically trained as a psychiatrist and completed a PhD program in clinical and experimental neuroscience at the University of Barcelona and a postdoctoral research fellowship with Dr. Brad Peterson at Columbia University, where he acquired expertise in advanced neuroimaging methods and cognitive neuroscience applied to the mechanistic study of cognition and learning in health and mental illness. He completed an NIMH K23 Research Career Development Award and he has published 35 peer-reviewed articles, 27 of them neuroimaging studies, and 15 of them as first or senior author. He currently directs a laboratory focused on cognitive and computational neuroscience and multimodal neuroimaging of psychosis ([www.columbiapsychiatry.org/research-labs/horga-lab](http://www.columbiapsychiatry.org/research-labs/horga-lab)). His lab is funded by federal and foundation grants, including two NIMH R01s. The lab currently includes a clinical rater, two research assistants, three post-doctoral fellows, one PhD student, and several undergraduate volunteers. His expertise, particularly focused cognitive and perceptual processes underlying psychosis, specifically in relation to computational modeling of Bayesian inference and predictive coding and development of targeted cognitive paradigms, is directly relevant to the neurocognitive core in the proposed U01. Additionally, he has expertise in the development, optimization, and validation of MRI-based biomarkers relevant to the neuroimaging and biomarkers in this U01 application. In particular, he has led work optimizing and validating neuromelanin-sensitive MRI as a marker of mesostriatal dopamine function that is able to capture alterations associated with psychosis.

* + 1. Baker SC, Konova AB, Daw ND, **Horga G**. A Distinct Inferential Mechanism for Delusions in Schizophrenia. *Brain* 2019 Mar 21. pii: awz051. doi: 10.1093/brain/awz051
    2. Cassidy CM, Zucca FA, Girgis RR, Baker SC, Weinstein JJ, Sharp ME, Bellei C, Valmadre A, Vanegas N, Kegeles LS, Brucato G, Jung Kang U, Sulzer D, Zecca L, Abi-Dargham A, **Horga G**. Neuromelanin-sensitive MRI as a noninvasive proxy measure of dopamine function in the human brain. *Proc Natl Acad Sci U S A* 2019 Mar 12;116(11):5108-5117. doi: 10.1073/pnas.1807983116. Epub 2019 Feb 22.
    3. Cassidy CM, Balsam PD, Weinstein JJ, Rosengard RJ, Slifstein M, Daw ND, Abi-Dargham A, **Horga G**. A Perceptual Inference Mechanism for Hallucinations Linked to Striatal Dopamine. Curr Biol. 2018 Feb 19;28(4):503-514.e4. doi: 10.1016/j.cub.2017.12.059. Epub 2018 Feb 2.
    4. Abi-Dargham A, **Horga G**. The search for imaging biomarkers in psychiatric disorders. *Nat Med*. 2016 Nov;22(11):1248-1255.

# Positions and Honors

# Positions and Employment

# 2018- Florence Irving Assistant Professor in Psychiatry, Columbia University, NY

# 2016- Assistant Professor in Psychiatry, SUNY Stony Brook, NY (voluntary appointment)

2013- Assistant Professor in Clinical Psychiatry, Columbia University, NY

2013- Research Scientist V, New York State Psychiatric Institute, RFMH, NY

2012-2013 Associate Research Scientist, Columbia University, NY

2009-2012 Post-doctoral research fellow, Columbia University, NY

2008 Visiting scholar, PET Lab, Mount Sinai School of Medicine, NY

2005-2009 Psychiatry Resident, Hospital Clínic of Barcelona, Spain

# Other Experience and Professional Memberships

# 2017- Doctoral Program in Neurobiology & Behavior, Columbia University, mentor

# 2017- American College of Neuropsychopharmacology (ACNP), associate member

# 2017- NYSPI MRI Unit Operations Committee, member

2009- Society for Neuroscience, member

2009- Organization for Human Brain Mapping, member

2009 Medical Trends S.L., Barcelona, Spain, scientific coordinator and translator

2009- PNAS, JAMA Psychiatry, Journal of Neuroscience, American Journal of Psychiatry, eLife, Brain, Neuropsychopharmacology, Biological Psychiatry, Human Brain Mapping, Neuroscience and Biobehavioral Reviews, Psychiatry Research: Neuroimaging, Schizophrenia Bulletin, Schizophrenia Research, European Psychiatry, Neuropsychologia, Expert Review of Neurotherapeutics, Journal of Child Psychology and Psychiatry, Frontiers in Human Neuroscience, Frontiers in Psychiatry, Journal of Psychiatric Research, ad-hoc reviewer

2013- Frontiers in Psychiatry, review editor

**Honors**

2018 BBRF Maltz Prize (for Innovative and Promising Schizophrenia Research)

2018 Irving Scholar Award

2017 Hot Topics Presentation at ACNP Annual Meeting

2016 RFMH Citronberg Fellowship

2016 Pisetsky Young Investigator Award

2015 Hot Topics Presentation at ACNP Annual Meeting

2015 Cum laude distinction for international PhD degree and nomination for outstanding award

2015 Parkinson’s Disease Foundation Panning Grant

2014 Sidney R. Baer, Jr. Foundation Seed Grant

2013 ACNP Travel Award

2012 Bodini fellowship award (Italian Academy for Advanced Studies in America, Columbia University, NY)

2009 Koplowitz fellowship award from the Alicia Koplowitz Foundation

2008 Spanish National Psychiatry Residents Prize

2007 Dr. Novoa Santos-Lilly Prize, Spanish National Psychiatry Meeting 2007

2005 Extraordinary Award in Medicine, Miguel Hernandez University, Spain (equivalent to summa cum laude)

# Contributions to Science

* 1. My early publications focused on novel or understudied treatments for severe mental illness, in particular schizophrenia spectrum disorders in treatment-resistant adolescents. These publications document the effectiveness of electroconvulsive therapy in early-onset schizophrenia while emphasizing potential side effects associated with treatments for refractory schizophrenia, including clozapine and electroconvulsive therapy. My more recent clinical work has contributed to the identification of clinical predictors of conversion to psychotic illness in clinical high-risk populations.
     1. **Horga G**, Horga A, Baeza I, Castro-Fornieles J, Pons A. Drug-induced speech dysfluency and myoclonus preceding generalized tonic-clonic seizures in an adolescent male with schizophrenia. *J Child Adolesc Psychopharmacol* 2010 Jun;20(3):233-234. PMID: 20578939
     2. Baeza I, Pons A, **Horga G**, Bernardo M, Lázaro ML, Castro-Fornieles J. Electroconvulsive therapy in early adolescents with schizophrenia spectrum disorders. *J ECT* 2009 Dec;25(4):278-279. PMID: 19384250
     3. Baeza I, Pons A, **Horga G**, Bernardo M, Lázaro ML, Castro-Fornieles J. Electroconvulsive therapy in early adolescents with schizophrenia spectrum disorders. *J ECT* 2009 Dec;25(4):278-279. PMID: 19384250
     4. Lehembre-Shiah E, Leong W, Brucato G, Abi-Dargham A, Lieberman JA, **Horga G**\*, Girgis RR\*. Distinct Relationships Between Visual and Auditory Perceptual Abnormalities and Conversion to Psychosis in a Clinical High-Risk Population. *JAMA Psychiatry*. 2017 Jan 1;74(1):104-106. PMID: 27851840 **\***Co-senior authors (Horga corresponding author).
  2. The bulk of my work has focused on the use of neuroimaging techniques to better understand the pathophysiology of schizophrenia, with an emphasis on psychotic symptoms, as well as to develop imaging biomarkers for severe mental disorders, including major depression and obsessive-compulsive disorders. In particular, my work using FDG-PET and fMRI has contributed to the understanding of the neural mechanisms of auditory verbal hallucinations in schizophrenia by showing increased activity in auditory cortex during silence in hallucinating patients in the absence of prior exposure to antipsychotic treatment, specifically in speech-sensitive regions of the temporal cortex. Furthermore, my research suggests that the neural mechanisms leading to this increased activity in the auditory cortex may result from deficits in sensory learning signals (specifically, deficits in sensory prediction errors) and striato-cortical dysconnectivity, supporting a model whereby deficits in predictive coding underlie hallucinations and psychosis more generally. In parallel, my recent work has pursued developing new MRI-based biomarkers relevant for psychosis. This work has included the validation of an MRI technique that provides a proxy measure for dopamine activity via high-resolution imaging of the substantia nigra.
     1. **Horga G**, Schatz, KC, Abi-Dagham A, Peterson BS. Deficits in Predictive Coding Underlie Hallucinations in Schizophrenia. *J Neurosci* 2014 Jun 11;34(24):8072-82. PMID: 24920613
     2. **Horga G**, Cassidy CM, Xu X, Moore H, Slifstein M, Van Snellenberg JX, Abi-Dargham A. Dopamine-Related Disruption of Functional Topography of Striatal Connections in Unmedicated Patients With Schizophrenia. *JAMA Psychiatry*. 2016 Aug 1;73(8):862-70. PMID: 27145361
     3. Cassidy CM, Balsam PD, Weinstein JJ, Rosengard RJ, Slifstein M, Daw ND, Abi-Dargham A, **Horga G**. A Perceptual Inference Mechanism for Hallucinations Linked to Striatal Dopamine. *Curr Biol*. 2018 Feb 19;28(4):503-514.e4. doi: 10.1016/j.cub.2017.12.059. Epub 2018 Feb 2. PMID: 29398218
     4. Cassidy CM, Zucca FA, Girgis RR, Baker SC, Weinstein JJ, Sharp ME, Bellei C, Valmadre A, Vanegas N, Kegeles LS, Brucato G, Jung Kang U, Sulzer D, Zecca L, Abi-Dargham A, **Horga G**. Neuromelanin-sensitive MRI as a noninvasive proxy measure of dopamine function in the human brain. *Proc Natl Acad Sci U S A* 2019 Mar 12;116(11):5108-5117. doi: 10.1073/pnas.1807983116. Epub 2019 Feb 22.
  3. In addition to clinically oriented neuroimaging work, part of my neuroimaging work has focused on the mechanisms of normal cognitive processes in health, including cognitive control, working memory and reinforcement learning. My work in cognitive control suggests that the dynamic interaction between systems representing the prior history of conflict and those responding to current conflict results in optimal, adaptive behavior. My work on reinforcement learning has provided empirical support to computational models of learning by showing that the functional connections between the striatum and sensorimotor systems strengthen as individuals learn the associations between contexts and optimal responses in those contexts.
     1. **Horga G**, Maia TV, Wang P, Wang Z, Marsh R, Peterson BS. Adaptation to conflict via context-driven anticipatory signals in the dorsomedial prefrontal cortex. *J Neurosci* 2011 Nov 9;31(45):16208-16.

PMID: 22072672; PMCID: PMC3244974

* + 1. **Horga G**, Maia TV. Conscious and unconscious processes in cognitive control: a theoretical perspective and a novel empirical approach. *Front Hum Neurosci* 2012 Jul 4 6:199. PMID: 23055959;

PMCID: PMC3458455

* + 1. **Horga G**, Maia TV, Marsh R, Hao X, Xu D, Duan Y, Tau GZ, Graniello B, Wang Z, Kangarlu A, Martinez D, Packard MG, Peterson BS. Changes in corticostriatal connectivity during reinforcement learning in humans. *Hum Brain Mapp* 2015 Feb;36(2):793-803. PMID: 25393839; PMCID: PMC4332407
    2. Van Snellenberg JX, Girgis RR, **Horga G**, van de Giessen E, Slifstein M, Ojeil N, Weinstein JJ, Moore H, Lieberman JA, Shohamy D, Smith EE, Abi-Dargham A. Mechanisms of Working Memory Impairment in Schizophrenia. *Biol Psychiatry*. 2016 Oct 15;80(8):617-26. PMID: 27056754

Complete list of published work: <http://www.ncbi.nlm.nih.gov/pubmed?term=Horga%20G>[Author]&cauthor=true&cauthor\_uid

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| **C. Research Support** |  |
| **Ongoing Research Support** |  |

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| **1R01MH117323** (Horga) | | 9/1/2018 - 6/30/2023 | | 0.60 | | CM | |
| NIH | $2,331,448 | |  | | TPE 0.18 CM | |  |
| Individualized risk prediction in persons at clinical high-risk for psychosis using neuromelanin-sensitive MRI | | | | | | | |
| We aim to test a new MRI-based biomarker that provides an objective measure of a well-known pathophysiological pathway in psychosis –the nigro-striatal dopamine dysfunction– to help identify individuals at clinical high risk who are particularly vulnerable to develop a full-blown psychotic disorder, and to use this objective biomarker to further improve individual risk predictions beyond those based solely on clinical data. | | | | | | | |
| Role: PI | | | | | | | |

**1R01MH114965** (Horga) 9/1/2018 - 6/30/2023 0.60 CM

NIH $2,386,572 TPE 0.18 CM

Deficient Belief Updating as a Convergent Computational Mechanism of Psychosis

This project aims to establish a novel model that integrates current clinical and neurobiological knowledge into a holistic model of psychosis explaining its common cognitive mechanism as well as symptom-specific pathways.

Role: Principal Investigator

**Dana Mahoney Neuroimaging** (Horga) 09/17/2015-09/16/2018

Dana Foundation

Title: Neuromelanin-sensitive MRI: development and validation of a novel dopamine biomarker for risk of

schizophrenia and Parkinson’s disease

The goal of this project is to validate and develop neuromelanin-sensitive MRI methods, and begin testing its feasibility as a novel dopamine biomarker for risk of schizophrenia and Parkinson’s disease.

Role: PI

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| **1 R21 MH110700-01** (Girgis, Horga)  NIMH | 09/01/2016- 08/31/2018 |

Title: Sensory-learning deficits and conversion to psychosis among individuals at clinical high-risk: a longitudinal model-based fMRI study

This fMRI study aims to establish whether abnormalities in predictive learning signals predict conversion to psychosis in subjects at clinical risk for psychosis.

Role: PI

**1R01 MH10935-01** (Abi-Dargham) 09/16/2016- 06/30/2021

NIMH

Title: Neurobiological correlates of auditory processing in health and disease: an RDoC study

The goal is to image dopamine release and identify molecular and neural correlates of auditory perceptual disturbances in psychosis.

Role: Co-I

**U01 NS098976** (Schroeder) 09/30/2016-8/31/2021

NIH

Title: Dynamic Neural Mechanisms of Audiovisual Speech Perception

The goal of the proposal is gain an understanding of the brain circuits and physiological processes underlying natural speech perception

Role: Co-I

**Completed Research Support**

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| **1 K23 MH101637** (Horga) NIMH | 06/01/2014-03/31/2019 |

Title: Neural mechanisms of sensory predictions in schizophrenia with hallucinations

The candidate proposes use computational models of learning to understand signaling of predictive signals in auditory systems and their relationship to auditory hallucinations in schizophrenia.

Role: PI