BIOGRAPHICAL SKETCH

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NAME: HAROON, EBRAHIM

eRA COMMONS USER NAME (credential, e.g., agency login): haroon2

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.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Madurai University Medical College, Madurai, India	MBBS	12/1980	Medicine and Surgery
Yale University-Department of Psychiatry, New Haven, CT	Postdoctoral Fellow	06/1998	Residency Training - Neuroscience Research Track
American Board of Psychiatry and Neurology (ABPN), Chicago, IL	Resident	present	Board Certification - Psychiatry (2001 - present),with Added Certification in Brain Injury Medicine - (2015 - present)

A. Personal Statement

Research focus: My primary scientific focus is in identifying treatment-resistance and in arresting the progressive functional decline among subjects with major psychiatric disorders by modulating immune and glutamate targets (citation #1). To achieve this goal, I use a combination of immune, imaging, cognitive and clinical phenotyping to identify and target pathologies afflicting inflammation, glutamate and glial systems (citation #2). **Career Trajectory:** I began my career in India by examining the vascular etiology of depressive disorders. I published one of the first reports on post-stroke depression in India in 1986. My continued work in this area exposed me to how silent progression of vascular pathology can lead to progressively worsening mood and cognitive symptoms. After immigrating to the United States in 1994, I joined residency training at the Clinical Neuroscience Research Program at Yale, where I learned how glutamate dysregulation in the brain could mediate the link between vascular disease and progressive brain diseases including depression. Following, my graduation from Yale, I had to take a break from academic pursuits to complete a 4-year obligatory service in rural Maine to overcome the constraints imposed by my visa status. In 2003, I rejoined academia by being recruited to UCLA and started retracing my steps under the auspices of the UCLA Late-Life Depression Research Program directed by Dr. Anand Kumar. As part of Dr. Kumar's Lab, I participated in multiple studies focussed on examining the role played in vascular pathology in the etiology of late-life depression. At Dr. Kumar's lab, I became interested in the application of magnetic resonance spectroscopy (MRS) in deciphering the glial and glutamate pathology associated with cerebrovascular disease. In 2006, I moved to Emory University in Atlanta (for personal reasons). At Emory, under the mentorship of Dr. Andrew Miller, I started examining how chronic immune activation might explain the link between vascular functions, metabolism, glutamate dysregulation, and depression (citation #4). During this period, I have worked on establishing glutamate dysregulation and glial pathology as critical mediators of immune-associated brain and behavior disorders. During my time at Emory, I was part of a first-of-a-kind clinical trial examining the role played by anti-cytokine therapy in the management of treatment-refractory depression (citation #3).

1. Haroon E, Miller AH. Inflammation Effects on Glutamate as a Pathway to Neuroprogression in Mood Disorders. Mod Trends Pharmacopsychiatry. 2017;31:37-55. PubMed PMID: 28738353.
2. Haroon E, Watari K, Thomas A, Ajilore O, Mintz J, Elderkin-Thompson V, Darwin C, Kumaran S, Kumar A. Prefrontal myo-inositol concentration and visuospatial functioning among diabetic depressed patients. Psychiatry Res. 2009 Jan 30;171(1):10-9. PubMed PMID: 19097871.

3. Ajilore O, Haroon E, Kumaran S, Darwin C, Binesh N, Mintz J, Miller J, Thomas MA, Kumar A. Measurement of brain metabolites in patients with type 2 diabetes and major depression using proton magnetic resonance spectroscopy. Neuropsychopharmacology. 2007 Jun;32(6):1224-31. PubMed PMID: 17180124.
4. Elderkin-Thompson V, Thomas MA, Binesh N, Mintz J, Haroon E, Dunkin JJ, Kumar A. Brain metabolites and cognitive function among older depressed and healthy individuals using 2D MR spectroscopy. Neuropsychopharmacology. 2004 Dec;29(12):2251-7. PubMed PMID: 15354181.

B. Positions and Honors

Positions and Employment

1987 - 1994	Assistant Professor of Psychiatry, Government of Tamil Nadu - Directorate of Medical Education, Madras University Medical Colleges, Chennai, India
1998 - 2001	Staff Psychiatrist - Washington County, Community Health & Counseling Services, Bangor, ME
2001 - 2002	Staff Psychiatrist, Kennebec Valley Mental Health Services, Waterville, ME
2003 - 2006	Assistant Professor & Attending Geriatric Psychiatrist, Department of Psychiatry and Biobehavioral Sciences, University of California at Los Angeles, Los Angeles, CA
2006 -	Assistant Professor, Department of Psychiatry and Behavioral Sciences, Emory University, Atlanta, GA
2014 -	Adjunct Assistant Professor, Wallace H Coulter Department of Biomedical Engineering , Georgia Institute of Technology, Atlanta, GA
2015 -	Adjunct Assistant Professor, Winship Cancer Institute, Emory University School of Medicine, Atlanta, GA
2016 -	Associate Director, Emory Behavioral Immunology Program, Winship Cancer Institute & Department of Psychiatry and Behavioral Sciences, Emory University, Atlanta, GA

Other Experience and Professional Memberships

1994 -	Life Fellow, Indian Psychiatric Society
2010 -	Member, (2010 -), Domestic Awards Committee (2010-2013) & Program Committee (2016 -), Society for Biological Psychiatry (SOBP)
2011 -	Study Section Memberships, ARRI-Phase 1 Study Section (2011), MESH Study Section (Ad hoc 2012), NIMH/Experimental Medicine-R21/R33 (2016), NPAS (2017), MESH (2018)
2012 - 2016	Member, Institutional Review Board, Emory University
2013 -	Member (non-office bearer), International Society for Magnetic Resonance In Medicine (ISMRM), Psychoneuroimmunology Research Society (PNIRS), International Society for CNS Trials in Medicine (ISCTM),

Honors

1997	Seymour L Lustman Resident Research Award, Yale University - Department of Psychiatry
1998	Paul E Kaunitz Award for Best Residency Performance in the Interface of Medicine and Psychiatry, Yale University
2005	Fellow, Summer Research Institute for Geriatric Psychiatry, University of California - San Diego & NIMH
2010	Young Investigator Award, National Association for Research on Schziophrenia and Affective Disorders
2011	Career Development Award, National Institute of Mental Health
2013	New Investigator Award, American Society for Clinical Psychopharmacology - NCDEU
2015	Fellow, Advanced Research Institute for Geriatric Mental Health, Cornell University & NIMH
2015	Editorial Board Member, Brain, Behavior & Immunity (published by PNIRS)

2016	Scientific Committee, Society for Biological Psychiatry, American Society for Clinical Psychopharmacology, Psychoneuroimmunology Research Society
2017	Co-Editor, Neuropsychopharmacology Reviews: "Behavioral Immunology in Psychiatry", Neuropsychopharmacology
2018	Co-Chair, Annual Conference Organizing Committee, Psychoneuroimmunology Research Society (International), Miami, FL, USA

C. Contribution to Science

1. **Psychoneuroimmunology of glutamate dysfunction:** Using support provided by NARSAD Young Investigator Award and K23 Award from NIMH, we demonstrated that inflammatory stimulation resulting from administration of interferon alpha for treatment of Hepatitis-C was associated with parallel increases in anterior cingulate and left basal ganglia glutamate increases, which in turn predicted severity of depression, motivational impairment and psychomotor slowing (citation #a). We later examined if the magnitude of inflammatory stimulation determined the extent of glutamate increases in a group of older subjects - who were known to demonstrate an exaggerated response to interferon alpha. This study showed that not only did glutamate elevations occur in tandem with exaggerated inflammatory response among older subjects, but this increase predicted the severity of behavioral impairments (citation #b). We further examined if chronic inflammatory activation seen among subjects with psychiatric disorders such as depression led to similar increases in glutamate. To our surprise, we not only found identical glutamate increases in the left basal ganglia regions among depressed patients who also showed high inflammation but that these increases predicted behavioral impairments such as anhedonia and psychomotor slowing (citation #c). Based on these and other evidence, we recently proposed a hypothesis that glutamate changes associated with inflammatory activation are different from glutamate alternations from other pathologies (such as stress) due to an increase in extrasynaptic glutamatergic activity (citation #d). We are currently testing this hypothesis in different contexts.

    a. Haroon E, Fleischer CC, Felger JC, Chen X, Woolwine BJ, Patel T, Hu XP, Miller AH. Conceptual convergence: increased inflammation is associated with increased basal ganglia glutamate in patients with major depression. Mol Psychiatry. 2016 Oct;21(10):1351-7. PubMed PMID: 26754953; PubMed Central PMCID: PMC4940313.

    b. Haroon E, Miller AH, Sanacora G. Inflammation, Glutamate, and Glia: A Trio of Trouble in Mood Disorders. Neuropsychopharmacology. 2017 Jan;42(1):193-215. PubMed PMID: 27629368; PubMed Central PMCID: PMC5143501.

    c. Haroon E, Felger JC, Woolwine BJ, Chen X, Parekh S, Spivey JR, Hu XP, Miller AH. Age-related increases in basal ganglia glutamate are associated with TNF, reduced motivation and decreased psychomotor speed during IFN-alpha treatment: Preliminary findings. Brain Behav Immun. 2015 May;46:17-22. PubMed PMID: 25500218; PubMed Central PMCID: PMC4414678.

    d. Haroon E, Woolwine BJ, Chen X, Pace TW, Parekh S, Spivey JR, Hu XP, Miller AH. IFN-alpha-induced cortical and subcortical glutamate changes assessed by magnetic resonance spectroscopy. Neuropsychopharmacology. 2014 Jun;39(7):1777-85. PubMed PMID: 24481242; PubMed Central PMCID: PMC4023151.

2. **Clinical outcomes relevant to the treatment of psychiatric disorders:** Available therapies for most neuropsychiatric disorders are useful only in a small sample of diagnosed subjects. In this regard, research focusses on molecules and pathology associated with treatment non-response including immune molecules (citations #c, d) and neurotransmitters such as glutamate (citation #b), dopamine (citation #a) and serotonin metabolites. We are testing these findings using pharmacological agents that modulate these chemicals.

    a. Haroon E, Daguanno AW, Woolwine BJ, Goldsmith DR, Baer WM, Wommack EC, Felger JC, Miller AH. Antidepressant treatment resistance is associated with increased inflammatory markers in patients with major depressive disorder. Psychoneuroendocrinology. 2018 May 19;95:43-49.

PubMed PMID: 29800779.

b. Goldsmith DR, Haroon E, Miller AH, Strauss GP, Buckley PF, Miller BJ. TNF-α and IL-6 are associated with the deficit syndrome and negative symptoms in patients with chronic schizophrenia. Schizophr Res. 2018 Feb 27;PubMed PMID: 29499967.

c. Haroon E, Miller AH. Inflammation Effects on Glutamate as a Pathway to Neuroprogression in Mood Disorders. Mod Trends Pharmacopsychiatry. 2017;31:37-55. PubMed PMID: 28738353.

d. Felger JC, Li Z, Haroon E, Woolwine BJ, Jung MY, Hu X, Miller AH. Inflammation is associated with decreased functional connectivity within corticostriatal reward circuitry in depression. Mol Psychiatry. 2016 Oct;21(10):1358-65. PubMed PMID: 26552591; PubMed Central PMCID: PMC4862934.

3. **Magnetic Resonance Spectroscopic (MRS) Approaches to the study of depression:** My personal research interests have focused on imaging brain response to activated peripheral inflammation in disorders of the mind and body. Towards this end, I have consistently spearheaded the employment of MRS technology as a sensitive tool in the understanding of the mind-body relationship. Our papers were among the earliest to demonstrate persisting glutamate abnormalities in the frontal and subcortical regions of older depressed patients (citations #a,#b,). This experience led to the very first report linking myoinositol (an astroglial marker) with cognitive functioning (citation #c) - a finding that has since been replicated with some consistency. Finally, we also demonstrated that alterations in glutamate and myo-inositol in the inflammatory biotype of depression might be a predictor of progressive decline (neuroprogression) and treatment resistance (citation #d).

   a. Haroon E, Miller AH. Inflammation Effects on Glutamate as a Pathway to Neuroprogression in Mood Disorders. Mod Trends Pharmacopsychiatry. 2017;31:37-55. PubMed PMID: 28738353.

   b. Haroon E, Watari K, Thomas A, Ajilore O, Mintz J, Elderkin-Thompson V, Darwin C, Kumaran S, Kumar A. Prefrontal myo-inositol concentration and visuospatial functioning among diabetic depressed patients. Psychiatry Res. 2009 Jan 30;171(1):10-9. PubMed PMID: 19097871.

   c. Ajilore O, Haroon E, Kumaran S, Darwin C, Binesh N, Mintz J, Miller J, Thomas MA, Kumar A. Measurement of brain metabolites in patients with type 2 diabetes and major depression using proton magnetic resonance spectroscopy. Neuropsychopharmacology. 2007 Jun;32(6):1224-31. PubMed PMID: 17180124.

   d. Elderkin-Thompson V, Thomas MA, Binesh N, Mintz J, Haroon E, Dunkin JJ, Kumar A. Brain metabolites and cognitive function among older depressed and healthy individuals using 2D MR spectroscopy. Neuropsychopharmacology. 2004 Dec;29(12):2251-7. PubMed PMID: 15354181.

4. **Neural circuitry changes in depressions associated with immune activation, diabetes, late-life and chronic vascular disease:** As part of Dr. Kumar's lab at UCLA, I participated in a wide variety of research studies focussing on linking cerebrovascular disease with depression and cognitive impairments. Our study was the among the first to employ 'surface contraction' analysis-based structural imaging to distinguish between late-life and early-life-onset depressions (b). We demonstrated anterior-posterior differences in pattern of atrophy predicting a strong link between late-life onset depressions and development of dementia. This study placed late-life onset depressions squarely within the pantheon of early dementias. Similarly, our team also published a pioneering report of grey matter changes in the orbitofrontal regions among diabetic patients with depression compared with non-depressed diabetic subjects and healthy controls (a). This orbitofrontal grey matter loss predicted delays in information processing as well. Another report from our group also further characterized vascular depressions using magnetic resonance spectroscopy (MRS)-derived metabolite subcortical and cortical brain changes (c). Finally, using retinal photography, our group demonstrated that depressed diabetic subjects exhibited greater dilatation of retinal arterioles compared with non-depressed diabetics and healthy controls (d). As seen above these pioneering studies elaborated a series of key mechanistic and diagnostic markers of relevance to the development of late life depressions.

   a. Ballmaier M, Narr KL, Toga AW, Elderkin-Thompson V, Thompson PM, Hamilton L, Haroon E,

Pham D, Heinz A, Kumar A. Hippocampal morphology and distinguishing late-onset from early-onset elderly depression. Am J Psychiatry. 2008 Feb;165(2):229-37. PubMed PMID: 17986679; PubMed Central PMCID: PMC2834288.

b. Haroon E, Watari K, Thomas A, Ajilore O, Mintz J, Elderkin-Thompson V, Darwin C, Kumaran S, Kumar A. Prefrontal myo-inositol concentration and visuospatial functioning among diabetic depressed patients. Psychiatry Res. 2009 Jan 30;171(1):10-9. PubMed PMID: 19097871.

c. Kumar A, Haroon E, Darwin C, Pham D, Ajilore O, Rodriguez G, Mintz J. Gray matter prefrontal changes in type 2 diabetes detected using MRI. J Magn Reson Imaging. 2008 Jan;27(1):14-9. PubMed PMID: 18050330.

d. Nguyen TT, Wong TY, Islam FM, Hubbard L, Ajilore O, Haroon E, Darwin C, Esser B, Kumar A. Evidence of early retinal microvascular changes in patients with type 2 diabetes and depression. Psychosom Med. 2010 Jul;72(6):535-8. PubMed PMID: 20368470.

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

Ongoing Research Support

R01MH112076, National Institute of Mental Health HAROON, EBRAHIM; MILLER, ANDREW H (PI) 09/23/16-07/31/21
Inflammation-Induced CNS Changes a A Function Of Depression.
The proposed study will examine if inflammation-induced anhedonia and psychomotor retardation in patients with major depressive disorder (MDD) and associated changes in basal ganglia glutamate concentrations and if these changes can be reversed following administration of anti-cytokine treatment with infliximab.
Role: CPI

R01 MH107033-01A1 HAROON, EBRAHIM (PI) 02/01/16-11/30/20
Inflammation-Induced CNS Glutamate as a Function of Depression in Middle Age
The proposed experiments will examine the link between increased white matter disease commonly seen among middle-aged depressed subjects with increased inflammation in the brain and plasma. Increased white matter disease has been associated with disease progression, treatment non-response and cognitive decline. Cutting-edge magnetic resonance imaging based spectroscopic and connectomic profiling will be used to characterize subjects at highest risk of progressive white matter disease, treatment non-response and cognitive impairments.
Role: PI

R01MH109637, National Institute for Mental Health FELGER, JENNIFER C (PI) 09/26/16-06/30/20
Inflammation Effects On Corticostriatal Connectivity And Reward: Role Of Dopamine
The proposed research will determine whether acute administration of the dopamine precursor levodopa will reverse functional connectivity changes in reward circuitry and associated anhedonic, psychomotor symptoms of major depressive disorder.
Role: Co-Investigator

R01MH108605, National Institute of Mental Health TREADWAY, MICHAEL T (PI) 07/20/16-03/01/21
Dynamics Of Inflammation And Its Blockade On Motivational Circuitry In Depression
Using a double-blind, placebo-controlled design, study will assess inflammation-induced motivational impairments and underlying corticostriatal circuit dysfunction in a patients with major depression will be reversed by cytokine-antagonist infliximab.
Role: Co-Investigator