BIOGRAPHICAL SKETCH

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NAME: Felger, Jennifer C.

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

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)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Florida, Gainesville, FL	B.S.	08/2001	Psychology
Emory University, Atlanta, GA	Ph.D.	05/2007	Neuroscience
The Rockefeller University, New York, NY	Postdoc	06/2009	Neuroimmunology
Emory University, Atlanta, GA	Postdoc	12/2012	Psychiatry
Emory University, Atlanta, GA	M.S.	05/2015	Clinical Research

A. Personal Statement

I study the impact of inflammation on neurotransmitters and neurocircuits in the brain that drive behavioral changes such as depression and fatigue. My work has established that inflammatory cytokines reduce striatal dopamine release, as measured in a non-human primate model of cytokine-induced depressive and anhedonic behavior (see Contribution #1). My training through the Emory KL2 and MSCR programs has provided didactic and practical experience in clinical research and functional neuroimaging to supplement my laboratory work investigating the immunologic mechanisms by which inflammation contributes to depression (e.g. Manuscripts #1 and 3). I have received NIH and foundation funding to investigate changes in neurocircuitry that may underlie inflammation-related behavioral symptoms in patients with major depression and in cancer patients undergoing treatment. Our recently published findings in depression suggest that increased inflammation is associated with decreased functional connectivity within dopaminergic corticostriatal circuits in relation with symptoms of reduced motivation and motor slowing (Manuscript #2). Currently I am examining whether these inflammation-related changes in reward and motor circuits are due to reductions in striatal dopamine using multimodal neuroimaging techniques, objective measures of motivation and motor function, and acute pharmacological challenge with levodopa. Together with my translational studies examining molecular and cellular mechanisms of inflammatory cytokine effects on neurotransmitters in post-mortem tissue from monkeys, this work will generate exciting new data relevant to novel pharmacological strategies for treating depression in patients with high inflammation.

1. Mehta D, Raison CL, Woolwine BJ, Haroon E, Binder EB, Miller AH, and **Felger JC**. (2013). Transcriptional signatures related to glucose and lipid metabolism predict treatment response to the tumor necrosis factor antagonist infliximab in patients with treatment-resistant depression. *Brain, Behavior, and Immunity.* 31:205-15. PMCID: PMC3673885
2. **Felger JC**, Li Z, Haroon E, Woolwine BJ, Jung MY, Hu X, Miller AH. (2016). Inflammation is associated with decreased functional connectivity within corticostriatal reward circuitry in depression. *Molecular Psychiatry* 21:1358-1365. PMCID: PMC4862934
3. **Felger JC**, Haroon E, Patel TA, Goldsmith DR, Wommack EC, Woolwine BJ, Le NA, Feinberg R, Tansey MG and Miller AH. What does plasma CRP tell us about peripheral and central inflammation in depression? *Molecular Psychiatry,* (accepted)

B. Positions and Honors

Positions and Employment

2007-2009 Fellow, Laboratory of Neuroendocrinology, The Rockefeller University, New York, NY
2009-2013 Fellow, Department of Psychiatry and Behavioral Sciences, Emory University, Atlanta, GA

2013- Laboratory Director, Emory Mind-Body Program, Winship Cancer Institute, Emory University, Atlanta, GA
2013- Assistant Professor, Department of Psychiatry and Behavioral Sciences, Emory University, Atlanta, GA
2013- Associate Member, Winship Cancer Institute, Emory University, Atlanta, GA

Other Experience and Professional Memberships

1998- Member, Psi Chi National Honor Society
2003- Member, Society for Neuroscience
2004- Member, Psychoneuroimmunology Research Society
2009 Certificate, Clinical and Translational Science, The Rockefeller University, New York, NY
2011- Reviewer, Ad-hoc: *Biological Psychiatry; Neuropsychopharmacology; Psychological Medicine; Psychoneuroendocrinology; PLoS ONE; Depression and Anxiety; Molecular Psychiatry; American Journal of Psychiatry; JAMA Psychiatry, Translational Psychiatry*
2011- Member, Society of Biological Psychiatry
2012 The Career Development Institute (CDI) for Psychiatry, University of Pittsburgh and NIMH
2013 Certificate, 3rd NIGMS-funded Short Course on Statistical Genetics & Genomics, University of Alabama at Birmingham, Birmingham, AL
2014- Member, American Society of Clinical Psychopharmacology (formerly NCDEU)
2015 Guest Co-Editor, *Physiology & Behavior*
2015- Editorial Board, *Brain, Behavior, and Immunity*
2016- Reviewer, Congressionally Directed Medical Research Programs (CDMRP) Gulf War Illness Research Program (GWIRP), Department of Defense
2017 Guest Co-Editor, *Neuropsychopharmacology Reviews*
2017 Grant Reviewer, Medical Research Council (MRC), UK
2017 Grant Reviewer, Health Research Board, Ireland
2017- *Ad-hoc* Reviewer, Neuroendocrinology, Neuroimmunology, Rhythms and Sleep (NNRS) Study Section, NIH
2018- Associate Member, American College of Neuropsychopharmacology
2018- Editorial Board, *Neuropsychopharmacology*

Selected Honors and Awards

2001-2004 Center for Behavioral Neuroscience (CBN) Scholarship, National Science Foundation and CBN Atlanta
2004-2007 Predoctoral Ruth L. Kirschstein National Research Service Award, NIMH
2005-2007 Achievement Rewards for College Scientists (ARCS) Scholar Award
2005-2007, 2009, 2011 Trainee Travel Awards, Psychoneuroimmunology Research Society
2010-2012 Postdoctoral Ruth L. Kirschstein National Research Service Award, NIMH
2012-2013 Glenn Family Breast Cancer Young Investigator Pilot, Winship Cancer Institute & Glenn Family
2013-2015 KL2 Mentored Clinical & Translational Research Scholarship, Atlanta Clinical and Translational Science Institute
2014 Burroughs-Wellcome Fund Trainee Travel Award, Association for Clinical and Translational Science
2014 New Investigator Award, American Society of Clinical Psychopharmacology (formerly NCDEU)
2014 Chairman's Choice Award, Society of Biological Psychiatry
2014 NARSAD Young Investigator Award, Brain and Behavior Research Foundation
2015 Travel Award, American College of Neuropsychopharmacology
2015 David Mahoney Neuroimaging Program New Investigator Grant, Dana Foundation
2016 Winter Conference on Brain Research Travel Fellowship
2017 Distinguished Scientific Contributions Award: Junior Faculty, Department of Psychiatry and Behavioral Sciences, Emory University
2017 Gerald Klerman Award for Clinical Research, Brain and Behavior Research Foundation

C. Contribution to Science

1. Inflammatory cytokines reduced motivation and motor activity by decreasing striatal dopamine. My work has demonstrated that chronic peripheral administration of interferon (IFN)-α reduces striatal dopamine release in a rhesus monkey model of inflammatory cytokine-induced depressive behavior. IFN-α-induced decreased in dopamine release correlated with decreased effort-based sucrose consumption, a measure of reduced motivation in monkeys, and were reversed by administration of the dopamine precursor, levodopa. I also discovered IFN-α-induced alterations in central and peripheral biomarkers of reduced dopamine

synthesis, which correlated with IFN-α-induced fatigue and reduced CSF dopamine, in patients receiving IFN-α for hepatitis C. Together, these findings have enhanced our understanding of how inflammatory cytokines affect the brain and dopamine to produce symptoms related to motivation and motor activity.

a. **Felger JC**, Alagbe O, Hu, F, Mook D, Freeman, AA, Sánchez MM, Kalin NH, Ratti E, Nemeroff CB and Miller AH. (2007). Behavioral, neuroendocrine, immune and neurotransmitter effects of interferon-alpha on rhesus monkeys: a non-human primate model of cytokine-induced depression. *Biological Psychiatry*. 62:1324-1333. PMCID: PMC2149847
b. **Felger JC**, Mun J, Kimmel HL, Nye JA, Drake DF, Hernandez CR, Freeman AA, Rye DB, Goodman MM, Howell LL, Miller AH. (2013). Chronic interferon-α decreases striatal dopamine release and dopamine 2 receptor binding in association with anhedonic behavior in non-human primates. *Neuropsychopharmacology,* 38:2179–2187. PMCID: PMC3773667
c. **Felger JC**, Li L, Marvar PJ, Woolwine BJ, Harrison DG, Raison CL, Miller AH. (2013). Tyrosine metabolism during interferon-α administration: Association with fatigue and CSF dopamine concentrations. *Brain, Behavior, and Immunity*. 31:153-60. PMCID:PMC3578984
d. **Felger JC**, Hernandez CR, Miller AH. (2015). Levodopa reverses cytokine-induced reductions in striatal dopamine release. *International Journal of Neuropsychopharmacology*. 18. PMCID: PMC4360218

2. Peripheral immunologic mechanisms of fatigue and depression in cancer and other medical illnesses. We have found that inflammatory genes and signaling pathways, e.g. p38 MAPK, NF-kB and viral response enzymes, predict development of fatigue and depressive symptoms in breast cancer patients following radiation and chemotherapy and in patients receiving IFN-α for hepatitis C virus. Additionally, we uncovered persistent inflammation-related epigenetic changes in peripheral immune cells of breast cancer patients following chemotherapy that were associated with increased concentrations of inflammatory cytokines. This work provided novel insights into the pathophysiology of inflammation-related fatigue and depression, including immunologic pathways that may serve as predictors or as potential targets for novel therapies.

a. **Felger JC***, Alagbe O*, Pace TWW, Woolwine BJ, Hu F, Raison CL, Miller AH. (2011). Relationship between the *in vivo* activation of p38 MAPK and the development of depressive symptoms during interferon-α therapy. *Brain, Behavior, and Immunity*. 25:1094-1098. *these authors contributed equally PMCID: PMC3116018
b. **Felger JC**, Cole SW, Pace TWW, Hu F, Woolwine BJ, Doho GH, Raison CL, Miller AH. (2012). Molecular signatures of peripheral blood mononuclear cells during chronic interferon-α treatment: relationship with depression and fatigue. *Psychological Medicine*. 42:1591-603. PMCID:PMC3433045
c. Torres MA, Pace TWW, Liu T, **Felger JC**, Mister D, Doho G, Kohn JN, Barsevick A, Long Q, Andrew AH. (2013). Predictors of depression in breast cancer patients during and after radiation: role of chemotherapy and nuclear factor kappa B. *Cancer*. 119:1951-9. PMCID:PMC3663885
d. Smith AK, Conneely KN, Pace TWW, Mister D, **Felger JC**, Kilaru V, Akel MJ, Vertino PM, Miller AH, and Torres MA. (2014). An epigenetic memory of prior chemotherapy associated with inflammation related to fatigue in breast cancer patients. *Brain, Behavior and Immunity* 38:227-36. PMCID: PMC4312666

3. The role of CD11c-expressing brain dendritic cells in health and disease. With a group of neuroscientists at The Rockefeller University, I examined the role of CD11c+ cells in the brain immune response following stroke in mice. Whereas CD11c-expressing dendritic cells from the periphery invaded regions of the necrotic ischemic core, resident CD11c-expressing cells of brain origin were activated and expressed in the border region of the infarct in close proximity to infiltrating T cells. I also contributed to two projects that determined these cells could become functional antigen presenting cells upon activation with IFN-gamma and that they accumulated in the brain during aging. These studies revealed that brain dendritic cells have the potential to mediate aspects of both innate and acquired immunity in the CNS.

a. Gottfried-Blackmore A, Kaunzner U, Idoyaga J, **Felger JC**, McEwen BS, and Bulloch K. (2009). Acute in vivo exposure to interferon-{gamma} enables resident brain dendritic cells to become effective antigen presenting cells. *Proceedings of the National Academy of Sciences*. 106:20918-23. PMCID:PMC2791588
b. **Felger JC**, Abe T, Kaunzner U, Gal-Toth J, Gottfried-Blackmore A, McEwen BS, Iadecola C, and Bulloch K. (2010). Brain dendritic cells in ischemic stroke: Time course, activation state, and origin. *Brain, Behavior, and Immunity*. 24:724-37. PMCID:PMC2885548
c. Kaunzner UW, Miller MM, Gottfried-Blackmore A, Kimura T, **Felger JC**, Gal-Toth J, McEwen BS, Bulloch K. (2012). Accumulation of resident and peripheral dendritic cells in the aging CNS. *Neurobiology of Aging*. 33:681-693. PMID:20692074D

4. Interactions between neuroendocrine, neuropeptide and immune systems in regard to behavior and stress responses. As an undergraduate at the University of Florida, I was the first of a team of three students to discover that intracerebroventricular injection of the neuropeptide orphanin FQ increased neophobic anxiety

behavior in rodents. As a graduate student at Emory, I investigated interactions between stress and sex steroid axes in relation to effects on neurotransmitter systems and anxiety behavior in monkeys, and contributed to a study that found a correlation between increased p38 MAPK inflammatory signaling in immune cells and decreased CSF serotonin metabolites in monkeys exposed to early life stress. This work served as a foundation for my developing interests in the effects of stress and immune activation on the brain and behavior.

a. Wilson ME, Mook D, Graves F, **Felger J**, Bielsky IF, Wallen K. (2003). Tamoxifen is an estrogen antagonist on gonadotropin secretion and responsiveness of the hypothalamic-pituitary- adrenal axis in female monkeys. *Endocrine*. 22:305-315.
b. Fernandez F, Misilmeri MA, **Felger JC**, Devine DP. (2004). Nociceptin/orphanin FQ increases anxiety-related behavior and circulating levels of corticosterone during neophobic tests of anxiety. *Neuropsychopharmacology*. 29:59-71.
c. Mook D, **Felger J**, Graves F, Wallen K and Wilson ME. (2005). Tamoxifen fails to affect central serotonergic tone but increases indices of anxiety in female rhesus macaques. *Psychoneuroendocrinology*. 30:273-83, 2005
d. Sánchez MM, Alagbe O, **Felger JC**, Zhang J, Graff AE, Grand AP, Maestripieri D and Miller AH. (2007). Activated p38 MAPK is associated with decreased CSF 5-HIAA and increased maternal rejection during infancy in young adult rhesus monkeys. *Molecular Psychiatry*. 12:895-7.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/jennifer.felger.1/bibliography/47408189/public/?sort=date&direction=ascending

D. Research Support

Ongoing

R01 MH108605 NIMH Felger (PI) 09/26/16-07/31/20
Inflammation effects on Corticostriatal Connectivity and Reward: Role of Dopamine
The proposal will test the hypotheses that increased inflammation in depression predicts improved connectivity in reward-related brain regions after acute pharmacological challenge with levodopa.
Role: PI

David Mahoney Neuroimaging Program Felger (PI) 09/17/15-09/16/19
The Dana Foundation
Using Pharmacological fMRI to Develop Novel Therapies for Treating Depression
The proposed research will use pharmacological fMRI to identify potential targets in the brain for future development of novel therapeutic strategies to treat depression in patients with high inflammation.
Role: PI

UG3 AT008857 NIH/NCCIH Rapaport (PI) 08/01/15-07/31/18
Omega-3 Fatty Acids for MDD with High Inflammation: A Personalized Approach
A randomized trial investigating the efficacy of omega-3 fatty acids monotherapy vs. placebo in subjects with major depression, obesity, and markers of inflammation.
Role: Co-I

NARSAD Distinguished Investigator Award Miller (PI) 01/01/18-12/31/19
Brain & Behavior Research Foundation
Cellular Immune Mechanisms of Inflammation in Depression
This project will use novel cell imaging techniques to examine the contribution of inflammatory myeloid cells to increased inflammation in patients with depression.
Role: Co-I

Completed (last 3 years)

R21 MH106904 NIH/NIMH Felger (PI) 08/01/15-05/31/18
Neurobiology of Cytokine effects on CNS Glutamate in IFN-α-Induced Depression
To elucidate novel strategies for treating inflammation-related depressive symptoms, this project will explore the role of the neurotransmitter glutamate using a translational model that has been shown to have direct relevance to cytokine-induced depression in humans.
Role: PI

NARSAD Young Investigator Award Felger (PI) 01/01/15-01/15/17
Brain & Behavior Research Foundation

The Neurocircuitry of Inflammation-Induced Anhedonia in Depression
This project will generate preliminary data to support the hypothesis that high inflammation in depression is associated with changes in neurocircuitry that are related to symptoms of anhedonia.
Role: PI

American Cancer Society Pilot Award Felger (PI) 06/01/15-05/31/16
Winship Cancer Institute ACS IRG Program
Inflammation-Induced Alterations in Neurocircuitry during Breast Cancer Treatment
This project will examine whether functional changes in basal ganglia and prefrontal cortical neurocircuitry underlie behavioral symptoms in breast cancer patients with persistent increases in inflammation after treatment.
Role: PI

University Research Committee Pilot Grant Felger (PI) 06/01/15-05/31/16
Emory University and the Atlanta Clinical and Translational Science Institute (ACTSI)
Inflammation-related Alterations in Corticostriatal Connectivity in Depression: Reversal with Levodopa
The goal of this pilot is to collect pilot data in support of the hypothesis that increasing dopamine precursors with levodopa can reverse inflammation-related decreases in functional connectivity within reward circuitry.
Role: PI

R21 AT007090 NIH/ NCCIH Rapaport (PI) 05/01/13-04/28/16
Efficacy of Swedish Massage Therapy on Cancer-Related Fatigue in Cancer Survivors
This study will investigate the biological and therapeutic effects of Swedish Massage Therapy (SMT) for cancer-related fatigue (CRF).
Role: Co-I

KL2 TR000455 ACTSI-RETCD Stephens (PI) 08/01/13-07/31/15
ACSTI Mentored Clinical & Translational Research Scholarship
Neurocircuitry of Cytokine-Induced Behavioral Change
Education in clinical research and biostatistics, and research experience and training in functional magnetic resonance imaging to examine the neurocircuitry that underlies inflammation-induced depressive symptoms.
Role: KL2 Scholar

Overlap
None