BIOGRAPHICAL SKETCH

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NAME: David Ryan Goldsmith

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

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Maryland, College Park MD	BS	05/2002	Psychology
Johns Hopkins University, Baltimore MD		05/2005	Pre-Medical Courses
Emory University, Atlanta GA	MD	05/2012	Medicine
Emory University, Atlanta GA	Residency	06/2016	Psychiatry
Emory University, Atlanta GA	MSCR	06/2019	Clinical and Translational Research

A. Personal Statement

My goal for this proposed American Diabetes Association Pathway Grant is to extend the focus of my research on inflammation in schizophrenia into novel and complementary areas pertaining to the association of anti-psychotic medications and diabetes and metabolic syndrome. My particular interests are to understand the mechanism of this association as it relates to inflammation, and ultimately towards prevention. This is of great relevance as anti-psychotic induced weight gain, dysglycemia, and cardiometabolic risk are significant contributors to the decreased life expectancy seen in these patients. I have had a longstanding interest in psychiatric research and schizophrenia since I was an undergraduate at the University of Maryland, where I studied schizotypal traits as a latent risk factor for the development of schizophrenia. I also spent a total of 4 years (2002-04 & 2008-10) in the Clinical Brain Disorders Branch at NIMH, working with Dr. Daniel Weinberger, focusing on the relationship between genetic risk factors for schizophrenia and cognition using neuroimaging to probe neurocognitive function. As a psychiatry resident on the research track at Emory, I became increasingly interested in the role of the immune system in schizophrenia. Currently, as an Assistant Professor, I am conducting research on inflammatory markers and negative symptoms, while seeing patients with persistent symptoms of schizophrenia and teaching residents and medical students about schizophrenia both in clinic and in the classroom.

My recently published meta-analysis of inflammatory cytokines across psychiatric disorders, including schizophrenia, has shaped the direction of my work.[1] Of note, this paper was highlighted in an NIH Request for Information (RFI NOT-MH-16-016). In addition, I have published a primary data paper demonstrating relationships between inflammatory cytokines and the deficit syndrome of schizophrenia, which is characterized by primary and enduring negative symptoms.[2] I also recently published a comprehensive review on the role of inflammation in schizophrenia.[3] Of relevance to this American Diabetes Association Pathways application, I have published a paper on the relationship between parental DM2 and risk for diabetes in individuals with non-affective psychosis, including schizophrenia.[4]

1. **Goldsmith DR**, Rapaport MH, Miller BJ. Meta-analysis of cytokine network alterations in psychiatric patients: comparisons between schizophrenia, bipolar disorder, and depression. *Molecular Psychiatry*. 2016 Dec; 21(12): 1696-1709. doi: 10.1038/mp.2016.3

2. **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. *Schizophrenia Research*. 2018 (epub ahead of print). doi: 10.1016/j.schres.2018.02.1048

3. Miller BJ & **Goldsmith DR**. Towards an immunophenotype of schizophrenia: Progress, potential mechanisms, and future directions. *Neuropsychopharmacology* 2017 Jan;42(1):299-317. doi: 10.1038/npp.2016.211.

4. Miller BJ, **Goldsmith DR**, Paletta N, Wong J, Kandhal P, Black C, Rapaport MH, Buckley PF. Parental type 2 diabetes in patients with non-affective psychosis. *Schizophrenia Research.* 2016 Aug;175(1-3):223-5. doi: 10.1016/j.schres.2016.04.035. PMC4958496

B. Positions and Honors

Positions and Employment

1998 – 2000 University of Maryland, College Park Scholars Program Citation, Life Sciences
2000 – 2002 Psychology Honors Program, University of Maryland College Park
2002 Bachelor of Science with Honors, University of Maryland College Park
2002 – 2004 Post-Baccalaureate Intramural Research Training Award, National Institute of Mental Health
2004 – 2005 Certificate, Johns Hopkins University Pre-Medical Post-Baccalaureate Program
2005 – 2006 Laboratory for Darwinian Neuroscience, Emory University Department of Anthropology
2008 – 2010 Pre-Doctoral Intramural Research Training Award, National Institute of Mental Health
2012 – 2016 Psychiatry Residency Program, Emory University Department of Psychiatry and Behavioral Sciences
2014 – 2016 Emory Department of Psychiatry Resident Research Track
2015 – 2016 Chief Resident, Research Track
2016 – Assistant Professor, Emory University Department of Psychiatry and Behavioral Sciences
2016 – Faculty, Emory Behavioral Immunology Program (Director: Andrew Miller, MD)
2016 – Associate Program Director, Psychiatry Residency Research Track, Emory University
2016 – Co-Director, Persistent Symptoms: Treatment, Assessment and Recovery (PSTAR) Clinic, Grady Memorial Hospital, Atlanta, GA

Other Experience and Professional Membership

2012 – American Psychiatric Association Member
2012 – Georgia Psychiatric Physicians Association Member
2013 – Medical Student Clinical Skills Examination Evaluator
2014 – Lecturer, Psychotic Disorders, M3 Medical Students
2015 –2016 Co-Director Psychotic Disorders Didactic Lecture Series for PGY1 and PGY2 Residents
2016 – Director Psychotic Disorders Didactic Lecture Series for PGY1 and PGY2 Residents
2015 – Co-Director Particle to Professor Lecture Series for PGY1 and PGY4 Residents
2015 – Emory Psychiatry Residency Education Committee Member
2015 – Ad hoc peer reviewer for: *American Journal of Psychiatry; Brain, Behavior, and Immunity; Current Psychiatry; International Journal of Molecular Sciences; International Journal of Emergency Mental Health; Journal of ECT; Journal of Nervous and Mental Disease; Molecular Psychiatry; Neuropsychopharmacology; Neuroscience and Biobehavioral Reviews; Psychopharmacology; Schizophrenia Bulletin; Schizophrenia Research; Scientific Reports*
2018 – Editorial Board Member, *Brain Behavior and Immunity*

Honors

2001 Omicron Delta Kappa, Sigma Circle, University of Maryland College Park
2002 Phi Beta Kappa, University of Maryland College Park
2010 Thompson Medical Scholarship, Emory University School of Medicine
2010 Harris Family Medical Scholarship, Emory University School of Medicine
2010 Wright-Bentley Medical Scholarship, Emory University School of Medicine
2013 American Psychiatric Institute for Research and Education/Janssen Resident Psychiatric Research Scholar
2014 NIMH Outstanding Resident Award Program, Honorable Mention
2014 Emory Department of Psychiatry Medical Student Teaching Award
2014 1st Place, Joe & Hope Skobba Memorial Award, Resident Research Competition, Georgia Psychiatric Physicians Association Annual Winter Meeting

2014 Janssen Academic Research Mentoring Program Award Recipient
2015 3rd Place, Joe & Hope Skobba Memorial Award, Resident Research Competition, Georgia Psychiatric Physicians Association Annual Winter Meeting
2015 American Society of Clinical Psychopharmacology New Investigator Award Program
2015 Walter Wellborn Endowed Fellowship Scholar
2016 Laughlin Fellow of the American College of Psychiatrists
2016 Career Development Institute (CDI) for Psychiatry Awardee, University of Pittsburgh
2016 1st Place, Joe & Hope Skobba Memorial Award, Resident Research Competition, Georgia Psychiatric Physicians Association Annual Winter Meeting
2016 2016 Emory Department of Psychiatry Resident Research Award
2017 Emory Department of Psychiatry PGY-1 Teaching Award
2017 National Institutes of Health Loan Repayment Program

C. Contributions to Science

1. Role of inflammation in major psychiatric disorders, including schizophrenia

In our meta-analysis of inflammatory cytokines in acute and chronic phases of major psychiatric illness, including schizophrenia, bipolar disorder, and major depressive disorder, we found a number of important similarities and differences in inflammatory cytokine concentrations between these disorders in different phases of illness. These data contribute to our understanding of the role of inflammation in psychiatric disorders and suggests that inflammation may be a viable treatment target for some patients. It also argues that as a field, we must have more uniformity in our study design and measurement of inflammatory cytokines in psychiatric illness. An invited review recently published in *Neuropsychopharmacology* highlights the complexity of inflammation's role in the pathogenesis of schizophrenia and suggests directions for future studies of inflammation in this disorder. I have also had a comprehensive review of biomarkers in schizophrenia, with a focus on inflammatory markers, including cytokines, as putative biomarkers of the disorder. Moreover, I recently published a paper demonstrating an association between tumor necrosis factor alpha (TNF-a) and interleukin (IL)-6 with the deficit syndrome of schizophrenia compared to non-deficit patients and healthy controls (manuscript under review). TNF-a also predicted blunted affect, alogia, as well as total negative symptoms.

a) **Goldsmith DR**, Rapaport MH, Miller BJ. Meta-analysis of cytokine network alterations in psychiatric patients: comparisons between schizophrenia, bipolar disorder, and depression. *Molecular Psychiatry* 2016 Dec; 21(12): 1696-1709. doi: 10.1038/mp.2016.3

b) Miller BJ & **Goldsmith DR**. Towards an immunophenotype of schizophrenia: Progress, potential mechanisms, and future directions. *Neuropsychopharmacology* 2017 Jan;42(1):299-317. doi: 10.1038/npp.2016.211.

c) **Goldsmith DR**, Crooks CL, Walker EF, Cotes RO. An update on promising biomarkers in schizophrenia. *FOCUS: The Journal of Lifelong Learning in Psychiatry.*

d) **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. *Schizophrenia Research*. 2018 (epub ahead of print). doi: 10.1016/j.schres.2018.02.1048

2. Contributions of metabolism and inflammatory markers to schizophrenia and factors associated with treatment resistance.

I recently published a paper with Dr. Brian Miller, where we explored the relationship between parental type-2 diabetes (DM2) and risk for diabetes in individuals with non-affective psychosis, including schizophrenia. It has been shown that metabolic disorders such as DM2 have a well-established relationship with increased inflammation. We found an increased prevalence of DM2 in parents of patients with non-affective psychosis compared to healthy controls; in addition, there was an increased odds of DM2 in patients with non-affective psychosis. I have also published three papers relevant to patients with treatment resistant schizophrenia – one making an argument for the need to screen for myocarditis in patients on clozapine, one exploring characteristics and predictors of antipsychotic polypharmacy, and one exploring the role of long acting injectable antipsychotics and suicide prevention.

a) Miller BJ, **Goldsmith DR**, Paletta N, Wong J, Kandhal P, Black C, Rapaport MH, Buckley PF. Parental type 2 diabetes in patients with non-affective psychosis. *Schizophrenia Research.* 2016 Aug;175(1-3):223-5. doi: 10.1016/j.schres.2016.04.035. PMC4958496

b) **Goldsmith DR**, Cotes RO. An Unmet Need: A Clozapine-Induced Myocarditis Screening Protocol. *Primary Care Companion for CNS Disorders.* 2017 Aug 3;19(4). doi: 10.4088/PCC.16l02083.

c) Cotes RO, **Goldsmith DR**, Kopelovich SK, Lally CA, Druss BG. Characteristics of Medicaid recipients receiving persistent antipsychotic polypharmacy. *Community Mental Health Journal*. 2017 (accepted).

d) Pompili M, Orsolini L, Lamis DA, **Goldsmith DR**, Nardella A, Falcone G, Corigliano V, Luciano M, Fiorillo A. Suicide prevention in schizophrenia: Do long-acting injectable antipsychotics (LAIs) have a role? *CNS and Neurological Disorders Drug Targets.* 2017 16(4):454-462. doi: 10.2174/1871527316666170223163629.

3. Impact of inflammation on behavior and cognition in patients with major depressive disorder

I published a paper with Dr. Andrew Miller, my primary mentor, exploring the role of inflammatory cytokines on neurocognitive tasks involving psychomotor speed in patients with major depression. We demonstrated a significant association between motor slowing on these tasks and plasma concentrations of pro-inflammatory markers, interleukin-6, and monocyte chemoattractant protein-1. Interleukin-10, an anti-inflammatory marker, was associated with faster performance on one of the psychomotor tasks. Importantly, we found that tasks with more of an attentional component were *unrelated* to inflammation. All of the psychomotor tasks have previously been shown to involve basal ganglia activity, and these data are consistent with and add to previous data demonstrating that inflammation can affect basal ganglia function. As such, psychomotor speed represents a viable outcome variable for future anti-inflammatory treatment trials in neuropsychiatric disorders characterized by increased inflammation. I have also recently published a paper demonstrating a relationship between peripheral inflammatory markers and number of failed antidepressant treatments trials. This suggests that inflammation may be associated with antidepressant treatment resistance. Measuring inflammatory markers and targeting inflammation or its downstream mediators may be relevant for patients with depression who have failed multiple antidepressant treatment trials. Also relevant to the impact of inflammation on behavior in depression is our recent chapter describing advances in the role of stress and inflammation in major depressive disorder.

a) **Goldsmith DR**, Haroon E, Woolwine BJ, Jung MY, Wommack EC, Harvey PD, Treadway MT, Felger JC, Miller AH. Inflammatory markers are associated with decreased psychomotor speed in patients with major depressive disorder. *Brain Behavior and Immunity.* 2016 Aug; 56:281-8. doi: 10.1016/j.bbi.2016.03.025. PMC4939278

b) Haroon E, Daguanno AW, Woolwine BJ, **Goldsmith DR**, Baer WM, Wommack EC, Felger JC, Miller AH. *Psychoneuroendocrinology*. 2018 May; 95:43-49. doi: 10.1016/j.psyneuen.2018.05.026.

c) **Goldsmith DR**, Cowles MK, Miller AH. Stress, Cytokines and Depressive Illness, In *Reference Module in Neuroscience and Biobehavioral Psychology*, Ed. Elsevier, 2016.

4. Role of neural networks in social cognition using fMRI based social reward task

In the year prior to starting medical school, I worked in the Laboratory for Darwinian Neuroscience in the Department of Anthropology at Emory University. Working with Dr. James Rilling, I co-authored three papers using fMRI to explore the neural networks that subserve social reward. This work contributes to our understanding of how the human brain has evolved to use reciprocal altruism in human interactions. Moreover, we were able to demonstrate how this system may adapt to in-group and out-group manipulations, as well as how it might be related to the construct of psychopathy.

a) Rilling JK, Glenn AL, Jairam MR, Pagnoni G, **Goldsmith DR**, Elfenbein HA, Lilienfeld SO. Neural correlates of social cooperation and non-cooperation as a function of psychopathy. *Biological Psychiatry*. 2007 Jun 1; 61(11): 1260-71.

b) Rilling JK, Degenais JE, **Goldsmith DR**, Glenn AL, Pagnoni G. Social cognitive neural networks during in-group and out-group interactions. *Neuroimage*. 2008 Jul 15; 41(4): 1447-61.

c) Rilling JK. **Goldsmith DR**, Glenn AL, Jairam MR, Elfenbein HA, Degenais JE, Murdock CD, Pagnoni G. The neural correlates of the affective response to unreciprocated cooperation. *Neuropsychologia*. 2008 Apr; 46(5): 1256-66.

Complete Bibliography of Published Work:
https://www.ncbi.nlm.nih.gov/sites/myncbi/1viQpeawtsAQJ/bibliography/40391497/public/?sort=date&direction=ascending

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C. Research Support

Ongoing Research Support

K23MH114037-01A1 Goldsmith (PI) 7/2/2018 – 6/30/2023
Under this K23 Mentored Career Development Award award, I will study the effects on inflammation on brain reward circuitry, motivational deficits, and negative symptoms and receive in depth training in fMRI, brain-immune interactions, and negative symptoms of schizophrenia to develop an independent research career.

U01 MH105573 Pato (PI) 7/30/2015-1/4/2019
Genomic Psychiatry Cohort (GPC): Genomic Parsing of Bipolar Disorder and Schizophrenia: Studies of Large Cohorts in the U.S.
Emory University will serve as a study site for a large genetic study of schizophrenia and bipolar disorder with the goal of recruiting 100 African American subjects with bipolar disorder or schizoaffective disorder, bipolar type.
Role: Co-Investigator (Rapaport, site PI)

Vanguard Research Group Kane (PI) 7/7/2015-4/20/2019
A Cluster, Randomized, Multi-center, Parallel-group, Rater-blind Study Comparing Treatment with Aripripazole Once Monthly and Treatment as Usual on Effectiveness in First Episode and Early Phase Illness in Schizophrenia
The goal of this project is to serve as a study site for the investigation of the use of a long acting injectable antipsychotic, Aripripazole, compared to treatment as usual in patients with first episode psychosis and early phase schizophrenia.
Role: Co-Investigator (Cotes, site PI)