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Dr. Cynthia Calkin

Correspondence language: English

Sex: Female

Date of Birth: 5/24

Canadian Residency Status: Canadian Citizen

Country of Citizenship: Canada, United States

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The primary information is denoted by (*)

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Primary Affiliation (*)

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Dr. Cynthia Calkin

Language Skills

Language	Read	Write	Speak	Understand	Peer Review
English	Yes	Yes	Yes	Yes	Yes
French	No	No	No	No	

Degrees

2010/6 - 2010/7	Diploma, Statistical Genetics: Probability and Statistical Inference, University of Washington Degree Status: Completed Supervisors: Dr. Bruce Weir
2010/6 - 2010/7	Diploma, The Peer Review Process & Making Your Grant More Competitive, Dalhousie University Degree Status: Completed Supervisors: Dr. Christopher McMaster
2005/7 - 2009/6	Doctorate, FRCPC - Fellow, Psychiatry, Dalhousie University Degree Status: Completed Supervisors: Dr. Malgorzata Rajda
1993/6 - 1995/6	Doctorate, CCFP - Fellow, Family Practice, Dalhousie University Degree Status: Completed Supervisors: Dr. Ian Cameron
1989/9 - 1993/6	Doctorate, M.D., Dalhousie University Degree Status: Completed Supervisors: Dr. Jock Murray
1987/9 - 1989/5	Bachelor's, BSc, cum laude, Dalhousie University Degree Status: Completed Supervisors: Dr. Jim Pincock

Credentials

2016/12	Member, Canadian College of Neuropsychopharmacology
2014/11	Member, International Society for Bipolar Disorders
2013/12	Member, American Psychiatric Association
2011/9	Member, International Group for the Study of Lithium

2009/6	FRCP, Fellow, Royal College of Physicians and Surgeons of Canada Psychiatry
2009/1	Member, Nova Scotia College Physicians & Surgeons Canada Psychiatry
2005/7	Member, Canadian Psychiatric Association
1995/7	Member, Canadian Medical Association
1995/6	CCFP, College of Family Physicians of Canada (The)
1994/1	Licensiate, MCCQE Part 1, Medical Council of Canada
1993/5	MD, Dalhousie University
1993/1	Licensiate, MCCQE Part 2, Medical Council of Canada
1999/1 - 2006/1	Certificant, American Board of Family Practice, American Board of Family Practice Family Practice

Recognitions

2016/12	Member Canadian College of Neuropsychopharmacology Honor
2014/12	Fellow American Psychiatric Association Honor
2014/10	Member, Task Force on Lithium International Society for Bipolar Disorders Honor
2010/10	Member International Group for the Study of Lithium (IGSLi) Honor
2009/9	Fellow Royal College of Physicians and Surgeons of Canada (The) Distinction
1999/1 - 2002/1	Physician's Recognition Award American Medical Association Distinction
1992/1	Dr Elizabeth Weld Memorial Award Dalhousie University Distinction
1991/1	John George & Emily MacDougall Award Dalhousie University Distinction
1990/1	John George & Emily MacDougall Award Dalhousie University Distinction
1989/5	Dean's Honor Role Dalhousie University Distinction

User Profile

Researcher Status: Researcher
Engaged in Clinical Research?: Yes

Key Theory / Methodology: Medical comorbidity such as insulin resistance may modify the course of bipolar illness, facilitating a more chronic neuroprogressive course with cognitive impairment (a more severe form of bipolar disorder). Treating underlying insulin resistance may be a key factor in improving psychiatric outcomes.

Research Interests: Medical co-morbidity in bipolar disorder has been my main focus of research. I am interested in the possible shared pathophysiology between bipolar disorder and medical co-morbidities (such as obesity, insulin resistance and type II diabetes, hypertension, cardiovascular disease). I am interested in the potential effect of medical co-morbidity on the blood-brain barrier, neuroinflammation and the effects on treatment response, course of illness and outcome in bipolar disorder.

Research Experience Summary: Obesity and bipolar disorder (BD): BD patients with elevated BMI had a chronic course and greater disability. Patients with BMI in the healthy range achieved complete remission on lithium, while those in the obese range had no response. Insulin resistance (IR) and type 2 diabetes (T2D) in BD: BD patients with IR/T2D are more likely to have a chronic course, not respond to lithium, have lower NAA and smaller hippocampal volumes compared to those without. Preliminary prospective results show that reversal of IR can improve BD outcome, but once diabetic, good glycemic control did not improve outcome. Treating insulin Resistance to Improve Outcome in BD: (ClinicalTrials.gov:NCT02519543) is a double-blind RCT of the efficacy of metformin in improving psychiatric outcomes in patients with IR and non-remitting bipolar depression. Blood-brain barrier dysfunction (BBBD) in BD: Using DCE-MRI we will determine whether IR and BBBD are associated with neuroprogression and cognitive impairment.

Fields of Application: Biomedical Aspects of Human Health, Pathogenesis and Treatment of Diseases

Disciplines Trained In: Psychiatry, Family Medicine

Areas of Research: Mood Disorders, Neuroendocrine Diseases

Research Specialization Keywords: Bipolar Disorder, Blood-brain barrier, Insulin Resistance, Medical neuroscience, Metabolic Syndrome, Neuroinflammation, Psychiatry, Type 2 Diabetes

Research Centres: Capital District Health Authority, Dalhousie University

Research Disciplines: Endocrinology, Neurosciences, Psychiatry

Employment

2016/7	Associate Professor Psychiatry, Medicine, Dalhousie University
2012/5	Assistant Professor Psychiatry, Medicine, Dalhousie University Term
2010/1	Lecturer Psychiatry, Medicine, Dalhousie University Term
2010/1	Staff Psychiatrist Psychiatry, Nova Scotia Health Authority
2005/1 - 2005/5	locum tenens, Family Practice Private Family Practice, Private Family Practice, Sandra Klynstra
2002/6 - 2004/12	Family Physician, owner Cynthia V. Calkin, MD, PLLC
1998/3 - 2002/5	Family Physician Physician's Immediate Care/ Medical Centers

1995/12 - 1997/11 Family Physician
Kennewick Family Medicine

1995/7 - 1995/9 locum tenens, Family Practice
Family Practice, The Moncton Medical Clinic

Affiliations

The primary affiliation is denoted by (*)

(*) 2016/7 Associate Professor, Psychiatry, Dalhousie University

2012/5 Assistant Professor, Psychiatry, Dalhousie University

2010/1 - 2012/5 Lecturer, Psychiatry, Dalhousie University

Research Funding History

Awarded [n=5]

2015/9 - 2020/8 Is type 2 diabetes mellitus a risk factor for neuroanatomical changes, cognitive impairment
Principal Investigator and oxidative stress in bipolar disorders?, Grant

Project Description: In this study, we will build on our previous work which will include not only neuroimaging and measures of cognitive functioning, but also measures of energy metabolism and oxidative stress. We will determine whether certain brain changes, memory impairment, and impaired energy metabolism/oxidative stress in bipolar disorder (BD) are associated with or exaggerated by type II diabetes mellitus (T2DM) and whether brain changes in BD and/or T2DM are related to impaired energy metabolism/oxidative stress.

Funding Sources:

2015/9 - 2020/8 Canadian Institutes of Health Research (CIHR)
Operating
Total Funding - 679,220 (Canadian dollar)
Funding Competitive?: Yes

Principal Applicant : Hajek, Tomas

2017/9 - 2019/9 Blood-brain barrier dysfunction as a diagnostic and pharmacodynamic biomarker for
Principal Applicant neuroprogressive bipolar disorder, Grant, Operating

Clinical Research Project?: Yes

Project Description: This is a cross-sectional case-control study to examine blood-brain barrier dysfunction (BBBD) using dynamic contrast enhanced magnetic resonance imaging (DCE-MRI), corresponding brain electrical activity using magnetoencephalography (MEG), and bipolar disorder (BD) outcome (neuroprogression), measured by overall morbidity using the Affective Morbidity Index and cognitive testing. We hypothesize that BBBD will be more frequent and to a greater extent in patients with BD and insulin resistance (IR) compared to those with BD without IR, IR-nonpsychiatric controls or healthy controls. We further predict that bipolar patients with BBBD will have a more advanced (neuroprogressive) course with greater overall morbidity and cognitive impairment compared to those without BBBD.

Research Settings: Canada (Both)

Research Disciplines: Psychiatry, Neurosciences, Biomedical Engineering and Biochemical Engineering, Endocrinology

Funding Sources:

2017/9 - 2019/9 Brain and Behavior Research Foundation
 NARSAD
 Total Funding - 133,000 (Canadian dollar)
 Funding Renewable?: No
 Funding Competitive?: Yes

Co-applicant : Alon Friedman;

Co-investigator : Chris Bowen; Martina Ruzickova; Matthias Schmidt; Tim Bardouille

2015/3 - 2018/2
 Principal Investigator Treating insulin resistance as a strategy to improve outcome in refractory bipolar disorder: a randomized, double-blind, placebo-control study of the efficacy of metformin in patients with insulin resistance and non-remitting bipolar illness., Grant
 Clinical Research Project?: Yes
 Project Description: In earlier studies we found that insulin resistance (IR) and type II diabetes mellitus (T2DM) were associated with a chronic course, more rapid cycling, poor response to lithium, unfavourable brain changes and neurocognitive deficits in bipolar patients. This proposed study will be the first to examine the efficacy of metformin as add-on treatment for improving outcome in patients with non-remitting bipolar disorder. Our hypotheses are that metformin will improve clinical outcome in BD and the degree of improvement in clinical outcome will correlate with the degree of improvement in IR. This will be a 26 week- randomized, double-blind, placebo-control study of the efficacy of metformin as add-on treatment in patients with IR and non-remitting bipolar illness, conducted over three years.

Research Settings: United States, Canada

Funding Sources:

2015/3 - 2018/11 Stanley Medical Research Institute (The)
 Treating insulin resistance as a strategy to improve outcome in refractory bipolar disorder: a RCT
 Total Funding - 1,315,221 (Canadian dollar)
 Funding Competitive?: Yes

Co-investigator : Martina Ruzickova

2017/5 - 2017/8
 Principal Applicant Blood-brain barrier dysfunction as a diagnostic and pharmacodynamic biomarker for neuroprogressive bipolar disorder Summer studentship, Grant
 Clinical Research Project?: Yes

Funding Sources:

2017/5 - 2017/8 Dalhousie Psychiatry Research Fund
 Total Funding - 4,000 (Canadian dollar) (Canadian dollar)
 Funding Renewable?: No
 Funding Competitive?: Yes

2016/6 - 2016/7
 Principal Applicant Treating insulin Resistance to Improve Outcome in Bipolar Disorder, Grant, Operating
 Clinical Research Project?: Yes
 Project Description: Double-blind RCT database

Funding Sources:

2015/6 - 2018/11 Dalhousie University
 Dalhousie Psychiatry Research Fund
 Total Funding - 13,330 (Canadian dollar)
 Funding Competitive?: Yes

Completed [n=4]

2016/5 - 2016/8 Principal Applicant	<p>Treating insulin Resistance as a strategy to Improve Outcome "TRIO-BD" study Summer studentship, Grant, Operating</p> <p>Project Description: Treating insulin Resistance as a strategy to Improve Outcome "TRIO-BD" study</p> <p>Funding Sources:</p> <p>Dalhousie Psychiatry Research Fund</p> <p>Total Funding - 4,000 (Canadian dollar) (Canadian dollar)</p>
2012/7 - 2016/1 Principal Investigator	<p>The risk and burden of insulin resistance in bipolar disorder, Grant, Operating</p> <p>Project Description: This is a study to examine type II diabetes mellitus (T2DM) and insulin resistance (IR, a precursor to T2DM) in patients with bipolar disorder (BD). BD appears to be a major risk factor for T2DM, comparable in magnitude to genetic factors, increasing risk two to three times compared to the general population. As a major risk factor, BD is highly relevant to understanding the mechanisms of T2DM and also for clinical care. Despite this increased risk in bipolar patients, there has been little diabetes research in this high risk population. We plan to establish the rate of IR in patients with BD and examine the impact of T2DM and IR on the clinical course and outcome of BD, including response to mood-stabilizing treatment. We will determine psychiatric and medical factors associated with an increased risk of IR and T2DM in 500 patients with BD. This will be the first step in establishing a research program to study medical comorbidity in BD.</p> <p>Funding Sources:</p> <p>2013/1 - 2015/1 Brain and Behavior Research Foundation (formerly known as NARSAD)</p> <p>Total Funding - 59,032 (United States dollar)</p> <p>Funding Competitive?: Yes</p>
2015/5 - 2015/8 Principal Applicant	<p>Treating insulin Resistance as a strategy to Improve Outcome "TRIO-BD" study Summer studentship, Grant, Operating</p> <p>Clinical Research Project?: Yes</p> <p>Project Description: Treating insulin Resistance as a strategy to Improve Outcome "TRIO-BD" study</p> <p>Funding Sources:</p> <p>2017/5 - 2017/8 Dalhousie Psychiatry Research Fund</p> <p>Total Funding - 4,000 (Canadian dollar) (Canadian dollar)</p> <p>Funding Renewable?: No</p> <p>Funding Competitive?: Yes</p>
2010/11 - 2012/8 Principal Investigator	<p>Sub-phenotyping bipolar disorder as a function of diabetes co-morbidity, Grant, Operating</p> <p>Clinical Research Project?: Yes</p> <p>Project Description: We propose to study sub-populations of patients with bipolar disorder (BD) with and without co-morbid diabetes mellitus. It remains to be established whether a clearly defined sub-group of patients with BD is associated with a greater risk of diabetes, metabolic syndrome, or other cardiovascular risk factors, or whether this risk is uniform across sub-groups. It is not known whether the presence of diabetes is associated with a poor response to specific treatment. There is a 3x increased risk of diabetes in patients with BD compared to the general population. The proposed study aims to better describe the clinical features and treatment response of sub-populations of patients with BD.</p>

Funding Sources:

2011/3 - 2012/8 Capital Health Research Fund
 Staff Award
 Total Funding - 14,949 (Canadian dollar)
 Funding Competitive?: Yes

Student/Postdoctoral Supervision**Bachelor's [n=1]**

2017/3 Claire Reardon (In Progress) , Dalhousie University
 Principal Supervisor Student Degree Start Date: 2015/9
 Student Degree Expected Date: 2019/5
 Student Canadian Residency Status: Canadian Citizen
 Thesis/Project Title: Treating Insulin resistance as a strategy to improve outcome in non-remitting bipolar disorder
 Present Position: Research assistant

 Project Funding Sources: Dalhousie Psychiatry Research Fund
 Amount - 4,000 (Canadian dollar)

Doctorate Equivalent [n=1]

2015/7 - 2017/5 Terry McCarvill (In Progress) , Dalhousie University
 Principal Supervisor Student Degree Start Date: 2012/7
 Student Degree Expected Date: 2017/5
 Student Canadian Residency Status: Canadian Citizen
 Thesis/Project Title: Retrospective study of the effect of insulin resistance and glycemic control on outcome in bipolar disorder disorder
 Project Description: This is a retrospective study of the relationship between insulin resistance (IR), glycemic control and outcome in 60 patients with bipolar disorder (BD) and IR ("pre-diabetes") or type II diabetes mellitus (T2DM) who have been prospectively followed in the Mood Disorders Program. In a cross-sectional study, we found that both IR and T2DM were associated with a greater severity of bipolar illness compared to those without metabolic disturbance. Bipolar patients with T2DM or IR were more likely to have a chronic course of illness and be refractory to treatment. Further, bipolar patients with IR had psychiatric outcomes that were *equally* as poor as those with T2DM. Insulin resistance may be an occult, modifiable risk factor for the most severe form of BD. It is a common metabolic disturbance with significant impact on BD outcomes. We expect that improvement in IR or glycemic control will be associated with an improvement in outcome in bipolar patients.
 Present Position: senior psychiatry resident

Research Associate [n=6]

2016/1 Peter Menzies (Completed) , Dalhousie University
 Principal Supervisor Thesis/Project Title: Treating insulin resistance as a strategy to improve outcome in non-remitting bipolar disorder
 Present Position: Research coordinator

2015/5 Principal Supervisor	Kathleen Cairns (In Progress) , Dalhousie University Student Degree Start Date: 2013/9 Student Degree Expected Date: 2017/5 Thesis/Project Title: 1) Treating Insulin resistance as a strategy to improve outcome in non-remitting bipolar disorder 2) Blood-brain barrier dysfunction as a diagnostic and pharmacodynamic biomarker for neuroprogressive bipolar disorder Present Position: Undergraduate student Project Funding Sources: Brain and Behavior Research Foundation Amount - 100,000 (United States dollar) ; Dalhousie Psychiatry Research Fund Amount - 8,000 (Canadian dollar) ; Stanley Medical Research Institute (The) Amount - 1,300,000 (Canadian dollar)
2014/5 - 2014/7 Co-Supervisor	Luca Steardo (Completed) , University of Naples Student Degree Start Date: 2011/9 Student Degree Received Date: 2015/6 Thesis/Project Title: Prospective study of the effect of insulin resistance and glycemic control on outcome in bipolar disorder Present Position: Full professor
2013/5 - 2014/5 Co-Supervisor	Zeina Asyyed (Completed) , Dalhousie University Student Degree Start Date: 2010/9 Student Degree Received Date: 2014/5 Thesis/Project Title: The risk and burden of insulin resistance in bipolar disorder Present Position: Medical student
2010/7 - 2010/12 Co-Supervisor	Sara Haak (Completed) , Technische Universität Dresden Student Degree Start Date: 2006/9 Student Degree Received Date: 2010/6 Thesis/Project Title: Sub-phenotyping bipolar disorder as a function of medical comorbidity Present Position: Psychiatrist
2010/6 - 2012/12 Co-Supervisor	Mirko Manchia (Completed) , University of Cagliari Student Degree Start Date: 2008/9 Student Degree Received Date: 2012/5 Thesis/Project Title: Study of the genetic basis of severe mental illness, such as bipolar disorder, and of pharmacogenetics/genomics of lithium. Present Position: Senior resident in psychiatry

Staff Supervision

Number of Scientific and Technical Staff: 8

Number of Visiting Researchers: 4

Number of Highly Qualified Personnel in Research Training: 3

Number of Personnel: 5

Number of Volunteers: 2

Editorial Activities

2016/5	Editorial Board Member, Bipolar Disorders- an International Journal of Psychiatry and Neurosciences, Journal Editorial Board Member, reviewer
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Mentoring Activities

2016/5	Associate Professor, Dalhousie University Number of Mentorees: 9 Mentorees: Crystal Zhou Anika Maraj Vanessa Bruckschwaiger Esther Rosenthal Shahzad Tanwir Zaki Shullah Ellie Fernandez Matthew Havenga Terry McCarvill Christie McClelland Darren Bennedict Clinical Mentor
2010/4	Research Mentor, Dalhousie University Number of Mentorees: 7 Mentorees: Kathleen Cairns Claire Reardon Terry McCarvill Sara Haak Zeina Asyyed Dorota Łojko Luca Steardo Research mentor
2012/6 - 2016/5	Assistant Professor, Dalhousie University Number of Mentorees: 28 Mentorees: Erinna Brown Catalina Lopez de Lara Sarah Smith Kathleen Singh Alyaa Abouzied Anne Sonley Leslie Kirkpatrick Josh Greene Maeghan Bebington Taylor Kallis Abraham Nunes Michael Fong Clinical Mentor
2010/1 - 2012/5	Lecturer, Dalhousie University Number of Mentorees: 13 Mentorees: Alice Aylott Natasha Snelgrove Martina Ruzickova Ava Miur Rachel Ottenbreit Deb Parker Victoria Wilkes Joanna Slusar Jonathan Brake Andras Papp Kurt Moyst Simon Bow Megan McLeod Clinical Mentor

Journal Review Activities

2016/8	Reviewer, Acta Psychiatrica Scandinavica Number of Works Reviewed / Refereed: 1
2015/3	Reviewer, Bipolar Disorders International Journal of Psychiatry and Neuroscience Number of Works Reviewed / Refereed: 2
2015/1	Reviewer, British Journal of Psychiatry Number of Works Reviewed / Refereed: 1
2014/10	Reviewer, Journal of Affective Disorders Number of Works Reviewed / Refereed: 3
2014/7	Reviewer, Depression and Anxiety Number of Works Reviewed / Refereed: 1
2013/12	Reviewer, Journal of Psychomatic Research Number of Works Reviewed / Refereed: 1
2012/8	Reviewer, Diabetology and Metabolic Syndrome Number of Works Reviewed / Refereed: 1
2011/2	Reviewer, Depression Research and Treatment Number of Works Reviewed / Refereed: 3
2010/6	Reviewer, The Canadian Journal of Psychiatry Number of Works Reviewed / Refereed: 1

2010/5	Reviewer, Psychiatry and Clinical Neurosciences Number of Works Reviewed / Refereed: 1
2009/2	Reviewer, Progress in Neuro-Psychopharmacology and Biological Psychiatry Number of Works Reviewed / Refereed: 2

Graduate Examination Activities

2012/4	Examiner, Department of Psychiatry, Dalhousie University
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Research Funding Application Assessment Activities

2016/10	Committee Member, Nova Scotia Health Authority Research Fund, Funder, Academic Reviewer, Nova Scotia Health Authority, Nova Scotia Health Authority Research Fund Number of Applications Assessed: 2
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Community and Volunteer Activities

2017/3	Clinical sub-specialist/researcher, The Nova Scotia Bipolar Peer Support Alliance Presentation of research findings on Mood and Metabolism, the TRIO-BD clinical Trial, blood-brain barrier research and the Mood and Metabolism Program in the Department of Psychiatry at Dalhousie University
2017/3	Clinical sub-specialist/researcher, Women in Psychiatry professional group Presentation of our Mood and Metabolism Program in the Department of Psychiatry at Dalhousie University
2015/5	Clinical subspecialist, Impact Ethics in Mental Health Public forum: Participant as invited guest in panel discussion on bipolar disorder
2014/11	Clinical sub-specialist/researcher, Women in Psychiatry professional group Presentation of insulin resistance and outcome in bipolar disorder and the "Treating insulin Resistance as a strategy to Improve Outcome in Bipolar Disorder (TRIO-BD)" study, a double blind RCT of the efficacy of metformin in treating non-remitting bipolar depression in bipolar patients with insulin resistance.
2014/5	Clinical subspecialist/ researcher, From Recovery To Discovery Mental Health Peer Support Group Presentation as invited guest: Diabetes and pre-diabetes predict lack of remission in bipolar disorder.
2012/11	Clinical subspecialist/ researcher, Women in Psychiatry professional group Presentation as invited guest: The role of early life adversity in bipolar disorder and diabetes.
2012/4	Clinical subspecialist/ researcher, The Nova Scotia Bipolar Peer Support Alliance - Halifax Chapter Presentation as invited guest: Bipolar Disorder and Metabolic Factors: Type 2 Diabetes, insulin resistance and metabolic syndrome.

Knowledge and Technology Translation

2017/2	Clinical researcher/ Consultant, Citizen Engagement Target Stakeholder: General Public Activity Description: Engage in knowledge translation with patients and public members in the Nova Scotia Bipolar Peer Support Alliance - Halifax Chapter
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2015/6	Clinical researcher/ consultant, Involvement in/Creation of Start-up Target Stakeholder: Healthcare Personnel Activity Description: Engage in knowledge translation of research findings in the form of a Registry Newsletter that goes out to patients, physicians and allied health care providers.
2014/10	Clinical researcher/ Consultant, Standards Development Target Stakeholder: Academic Personnel Activity Description: Consultant for the International Society for Bipolar Disorders Task Force for setting standards of care for the use of lithium
2013/10	Clinical researcher/ Consultant, Involvement in/Creation of Start-up Target Stakeholder: Healthcare Personnel Activity Description: Founder of the Mood and Metabolism Program, Dalhousie University. This program has both research and clinical components.

International Collaboration Activities

2017/1	Researcher, co-investigator, PGBD memberUnited States Pharmacogenomics of mood stabilizer response in bipolar disorder (PGBD) international study with Dr John Kelsoe, PI
2015/10	Researcher, IGSLi member, Germany Research collaboration, International Group for the Study of Lithium treated patients (IGSLi)
2015/4	Researcher, principal investigator, Italy Research collaboration with Palmiero Monteri: Prospective study of the effect of insulin resistance and glycemic control on outcome in bipolar disorder
2014/12	Researcher, co-investigator, Italy Research collaboration with Leonardo Tondo: Long-term effects of lithium on renal function
2014/11	Researcher, clinical expert, ISBD member, United States International Society for Bipolar Disorders Task Force member/advisor for international treatment guidelines for the use of lithium in bipolar disorder
2014/11	Researcher, principal investigator, sponsor, United States Research collaboration with Roy Chengappa: Treating insulin Resistance as a strategy to Improve Outcome in refractory Bipolar Disorder: a randomized, double-blind, placebo-control study of the efficacy of metformin in patients with insulin resistance and non-remitting bipolar illness (TRIO-BD study) ClinicalTrials.gov: NCT02519543
2013/4 - 2014/4	Researcher, co-investigator, Poland Research Collaboration with Dorota Lojko - Metabolic Disorders and Cognition Study

Committee Memberships

2015/5	Group Chair, Department of Psychiatry, Dalhousie University Clinical Trials: working group for strategic planning
2015/4	Committee Member, Department of Psychiatry, Dalhousie University Research Strategic Planning Sub-committee, Dalhousie University
2015/1	Committee Member, Department of Psychiatry, Dalhousie University Research Committee, Dalhousie University

Other Memberships

2016/5 Editorial Board Member, Bipolar Disorders International Journal of Psychiatry and Neuroscience

Most Significant Contributions

The risk and burden of insulin resistance in bipolar disorder
We found high rates of IR and type 2 diabetes (T2D) in BD patients- 3x that of the general population. More than half of all BD patients have IR/T2D. We made the important discovery that comorbid IR or T2D was associated with poor outcome in BD. Bipolar patients with IR or T2D are 3x more likely to have a chronic course of illness ($p=0.0007$) and 8x more likely not to respond to mood stabilizing treatment ($p<0.0001$). Further, BD patients with IR had equally poor outcomes as those with T2D, suggesting that it might be important to intervene at the IR stage. C. Calkin, M. Řůžicková, et al. Insulin resistance and outcome in bipolar disorder. Br J Psychiatry 206: 52-7, 2015

Treating insulin resistance in bipolar patients with non-remitting illness may be a new strategy for achieving remission.

It is a novel concept to consider treating an underlying metabolic disorder in order to improve a psychiatric one. In 2014, I was awarded \$1.3 million from the Stanley Medical Research Institute to study this. I am the Principal Investigator and Sponsor for my "Treating insulin Resistance as a strategy to Improve Outcome in Bipolar Disorder (TRIO-BD)" study, a randomized double-blind placebo-controlled trial of the efficacy of metformin in treating patients with IR and non-remitting BD.

Brain changes on neuroimaging bipolar patients likely due to comorbid insulin resistance or type 2 diabetes

As a Co-Principal Investigator on a CIHR-funded study we have determined that abnormal brain changes found on neuroimaging BD patients are likely due to comorbid IR/T2D and not due to BD, per se. T. Hajek, C. Calkin, et al. Insulin resistance, diabetes mellitus and brain structure in bipolar disorders. Neuropsychopharm 39 (12): 2910-8, 2014 T. Hajek, C. Calkin, et al. Type 2 diabetes mellitus - a potentially modifiable risk factor for neurochemical brain changes in bipolar disorders. Biol Psychiatry 77 (3): 295-303, 2015

Insulin resistance and bipolar disorder leads to a change in clinical care.

Publication of our results immediately led to questions globally regarding how this should impact clinical care, and I was asked by the editors of Bipolar Disorders to address this.

Our results were compelling enough to recommended yearly screening for IR in BD patients, leading to a change in approach to clinical care. C. Calkin, M. Alda. Insulin resistance in bipolar disorder - relevance to routine clinical care. Bipolar Disord 17 (6): 583-8, 2015 Further, based on our results, bipolar disorder is now considered an independent risk factor for type 2 diabetes by the Canadian Diabetes Association.

2009/9

Obesity in bipolar disorder might predict outcome

C. Calkin, C. van de Velde, M. Řůžicková, C. Slaney, J. Garnham, T. Hajek, C. O'Donovan, M. Alda. Can body mass index help predict outcome in patients with bipolar disorder? Bipolar Disorders, 2009 Sep; 11 (6): 650 - 656. Bipolar patients with comorbid obesity have a more chronic course of illness and poor outcomes. Those with body mass index (BMI) in the obese range had complete remission of their bipolar disorder on lithium, while those in the obese range had no clinical response. This lead to recommendations to monitor BMI and metabolic parameters in the national (CANMAT) guidelines for treatment of bipolar disorder.

Presentations

1. Calkin C. (2017). Childhood trauma is associated with comorbid insulin resistance, type 2 diabetes and poor response to lithium in adults with bipolar disorder. International Society for Bipolar Disorders, Washington, DC, United States
Main Audience: Researcher, Competitive?: Yes
Funding Sources: Brain and Behavior Research Foundation; Capital Health Research Fund
2. Calkin C. (2017). Mood and Metabolism. Women in Psychiatry group,
Main Audience: Knowledge User
Invited?: Yes
3. Calkin C. (2016). Insulin resistance takes center stage: a new paradigm in the progression of bipolar disorder. International Society for Bipolar Disorders/Affective Disorders annual meeting, Amsterdam, Netherlands
Main Audience: Researcher
Invited?: No, Keynote?: No
4. Calkin C, Garnham J. (2016). Pearls of wisdom: responsibilities of developing a drug trial. Centre for Clinical Research, Dalhousie University, Halifax, Canada
Main Audience: Knowledge User
Invited?: Yes
5. Calkin C. (2016). Insulin resistance takes center stage in the progression of bipolar disorder. Women in Psychiatry group, Halifax, Canada
Main Audience: Knowledge User
Invited?: Yes
6. Calkin C. (2016). Treating insulin Resistance as a strategy to Improve Outcome in Bipolar Disorder. East Coast Forensic Hospital, Clinical Academic Rounds, Dalhousie University, Halifax, Canada
Main Audience: Knowledge User
Invited?: Yes, Keynote?: No
7. Calkin C, Řůžičková M, Uher R, Hajek T, Slaney C, Garnham J, O'Donovan MC, Alda M. (2015). Co-morbid insulin resistance may be an important factor in non-remitting bipolar disorder. Canadian Psychiatric Association annual meeting, Vancouver, Canada
Main Audience: Knowledge User
Invited?: No, Keynote?: No, Competitive?: Yes
8. Calkin C, Řůžičková M, Uher R, Hajek T, Slaney C, Garnham J, O'Donovan MC, Alda M. (2015). Insulin resistance and outcome in bipolar disorder. Atlantic Provinces Psychiatric Association annual meeting, St. John's, Canada
Main Audience: Knowledge User, Competitive?: Yes
9. Calkin C. (2015). Treatment resistant bipolar disorder: new strategies for achieving remission. Clinical Academic Rounds, Department of Psychiatry, Dalhousie University, Halifax, Canada
Main Audience: Knowledge User
Invited?: No, Keynote?: No
10. Calkin C, Hajek T. (2015). Insulin resistance: the culprit behind chronic course, treatment resistance, cognitive impairment and brain abnormalities in bipolar disorder?. Clinical Academic Rounds, Department of Psychiatry, Dalhousie University, Halifax, Canada
Main Audience: Knowledge User
11. Calkin C. (2015). Insulin resistance and bipolar disorder. Pre-diabetes and Mental Health Conference, McGill University and Douglas Mental Health Institute, Montreal, Canada
Main Audience: Researcher
Invited?: Yes, Keynote?: No

12. C. Calkin. (2014). Insulin resistance: An occult, modifiable risk factor for refractory bipolar disorder. International College of Neuropsychopharmacology (CINP) World Congress, Canada
Main Audience: Researcher
Invited?: No, Keynote?: No, Competitive?: Yes
13. Calkin C, Alda M. (2014). Prospective study of the effect of insulin resistance on outcome in lithium-treated patients with bipolar disorder. International Group for the Study of Lithium-treated patients (IGSLi) annual meeting, Poznan, Poland
Main Audience: Researcher
14. Calkin, C. (2014). Co-morbid insulin resistance and type II diabetes predict chronic course of bipolar illness and poor response to lithium. American Psychiatric Association Annual meeting, United States
Main Audience: Knowledge User
Invited?: No, Keynote?: No
15. Calkin C. (2013). Are co-morbid insulin resistance and type II diabetes risk factors for refractory bipolar illness?. European Congress of Neuropsychopharmacology (ECNP), Barcelona, Spain
Main Audience: Researcher
Invited?: No, Keynote?: No, Competitive?: Yes
16. Calkin C, Růžicková M, Uher R, Slaney C, Garnham J, O'Donovan C, Alda M. (2013). Co-morbid insulin resistance and type II diabetes may predict poor response to lithium in patients with bipolar disorder. Dalhousie University, Department of Psychiatry, Research Day, Halifax, Canada
Main Audience: Researcher, Competitive?: Yes
17. Calkin C, Alda M.(2013). Co-morbid insulin resistance and type II diabetes may predict poor response to lithium. 2013 International Group for the Study of Lithium treated patients (IGSLi) annual meeting, Dresden, Germany
Main Audience: Researcher
Invited?: Yes, Keynote?: No, Competitive?: Yes
18. Calkin C. (2013). Treatment of refractory bipolar disorder. Nova Scotia College of Nurse practitioners presented as invited guest, Halifax, Canada
Main Audience: Knowledge User
Invited?: Yes
19. Calkin C.(2012). Metabolic abnormalities in bipolar disorder. 2012 New Brunswick Psychiatric Association Annual Meeting, Moncton, Canada
Main Audience: Knowledge User
Invited?: Yes
20. Calkin C.(2012). Medical Co-morbidity in Bipolar Disorder and the Role of Early Life Adversity. Clinical Academic Rounds Queen Elizabeth II Health Sciences Centre, Halifax, Canada
Main Audience: Knowledge User
21. Calkin C. (2012). The risk and burden of insulin resistance and type 2 diabetes in bipolar disorder. International College of Neuropsychopharmacology (CINP) World Congress, Sweden
Main Audience: Researcher
Invited?: No, Keynote?: No, Competitive?: Yes
22. Calkin C, Van de Velde C, Růžicková M, Slaney C, Garnham J, Hajek T, O'Donovan C, Alda M.(2011). Can body mass index help predict prognosis and outcome in bipolar disorder?. World Congress of Biological Psychiatry (WFSBP) Annual Meeting, Czech Republic
Main Audience: Researcher, Competitive?: Yes
23. Calkin C. (2010). Diabetes and metabolic factors in bipolar disorder. International Group for the Study of lithium treated patients (IGSLi) annual meeting (invited guest), Cagliari, Italy
Main Audience: Researcher
Invited?: Yes, Keynote?: No

24. Calkin C.(2010). Sub-phenotyping Bipolar Disorder as a Function of Diabetes Co-morbidity. Canadian Institutes of Health Research: New Principal Investigators Meeting, Jackson's Point, Canada
Main Audience: Researcher
Invited?: Yes
25. Calkin C, Van de Velde C, Řůžicková M, Slaney C, Garnham J, Hajek T, O'Donovan C, Alda M.(2009). Body mass index correlates of bipolar disorder: Can BMI help predict prognosis and outcome?. Society of Biological Psychiatry (SOBP) Annual Meeting, Vancouver, Canada
Main Audience: Researcher, Competitive?: Yes
26. Calkin C, Van de Velde C, Řůžicková M, Slaney C, Garnham J, Hajek T, O'Donovan C, Alda M.(2009). Body mass index correlates of bipolar disorder: Can BMI help predict prognosis and outcome?. World Congress of Biological Psychiatry (WFSP) Annual Meeting, Paris, France
Main Audience: Researcher, Competitive?: Yes
27. Calkin C, Van de Velde C, Řůžicková M, Slaney C, Garnham J, Hajek T, O'Donovan C, Alda M.(2008). Body mass index correlates of bipolar disorder: Can BMI help predict prognosis and outcome?. American Psychiatric Association Annual Meeting, District of Columbia, United States
Main Audience: Knowledge User, Competitive?: Yes

Broadcast Interviews

Bipolar disorder and metabolic comorbidity, CIOE, FM radio, George Jordan

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Text Interviews

- | | |
|------------|---|
| 2014/05/04 | Calkin C, et al. Co-morbid insulin resistance and type II diabetes predict chronic course of bipolar illness and poor response to lithium, American Psychiatric Association Annual Meeting, New York City, 2014 |
| 2008/05/05 | Calkin C, et al. Can body mass index help predict outcome in patients with bipolar disorder?, American Psychiatric Association Annual meeting, Washington DC 2008 |

Publications

Journal Articles

1. Ketil J. Oedegaard, Martin Alda, Anit Anand, Ole A. Andreassen, Yakesh Balaraman, Wade H. Berrettini, Abesh Bhattacharjee, Kristen J. Brennand, Katherine E. Burdick, Joseph R. Calabrese, Cynthia V. Calkin, Ana Claasen, William H. Coryell, David Craig, Anna DeModena, Mark Frye, Fred H. Gage, Keming Gao, Julie Garnham, Elliot Gershon, Petter Jakobsen, Susan G. Leckband, Michael J. McCarthy, Melvin G. McInnis, Adam X. Maihofer, Jerome Mertens, Gunnar Morken, Caroline M. Nievergelt, John Nurnberger, Son Pham, Helle Schoeyen, Tatyana Shekhtman, Paul D. Shilling, Szabolcs Szelinger, Bruce Tarwater, Jun Yao, Peter P. Zandi, and John R. Kelsoe. (2016). The Pharmacogenomics of Bipolar Disorder study (PGBD): identification of genes for lithium response in a prospective sample. *BMC Psychiatry*. 16(129): 1-15.
<http://dx.doi.org/10.1186/s12888-016-0732->
 Co-Author
 Published,
 Refereed?: Yes
 Number of Contributors: 38
 Description of Contribution Role: 2016; 16: 129. Published online 2016 May 5. doi:
 Description / Contribution Value: I am a co-investigator for the Pharmacogenomics of Bipolar Disorder study
2. Ilves P, Ilves L, Calkin C. (2016). The role of film in public perception of bipolar disorder: perpetuating stigma in *Silver Linings Playbook*. *Journal of Ethics in Mental Health*. open: 1-4.
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3. Calkin C. (2016). Insulin resistance takes center stage: a new paradigm in the progression of bipolar disorder?. *Bipolar Disorders*.
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4. Leonardo Tondo, Maria Abramowicz, Martin Alda, Michael Bauer, Alberto Bocchetta, Lorenza Bolzani, Cynthia V. Calkin, Caterina Chillotti, Diego Hidalgo-Mazzei, Mirko Manchia, Bruno Müller-Oerlinghausen, Andrea Murru, Giulio Perugi, Marco Pinna, Giuseppe Quaranta, Daniela Reginaldi, Andreas Reif, Philipp Ritter, Janusz K. Rybakowski, David Saiger, Valerio Selle, Thomas Stamm, Gustavo H. Vázquez, Eduard Vieta, Julia Volkert, and Ross J. Baldessarini. (2016). Long-term lithium treatment in bipolar disorder: Effects on GFR and other metabolic parameters. *International Journal of Bipolar Disorders*.
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 Number of Contributors: 26
 Contribution Percentage: 11-20
 Description of Contribution Role: Co-Author
5. Propper L, Ortiz A, Slaney C, Garnham J, Růžicková M, Calkin C, O'Donovan C, Hajek T, Alda M. (2015). Early-onset and very-early-onset bipolar disorder: distinct or similar clinical conditions?. *Bipolar Disorders*. 17: 814-820.
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6. Jerome Mertens, Qiu-Wen Wang, Yongsung Kim, Diana X. Yu, Son Pham, Bo Yang, Yi Zheng, Kenneth E. Diffenderfer, Jian Zhang, Sheila Soltani, Tameji Eames, Simon T. Schafer, Leah Boyer, Maria C. Marchetto, John I. Nurnberger, Joseph R. Calabrese, Ketil J. Ødegaard, Michael J. McCarthy, Peter P. Zandi, Martin Alba, Caroline M. Nievergelt, The Pharmacogenomics of Bipolar Disorder Study†, Shuangli Mi, Kristen J. Brennand, John R. Kelsoe, Fred H. Gage & Jun Yao. (2015). Differential responses to lithium in hyperexcitable neurons from patients with bipolar disorder . Nature. doi:10.1038/nature15(5): 1-16.
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7. Hajek T , Calkin C , Blagdon R , Slaney C , Alda M. (2015). Type 2 Diabetes Mellitus: A Potentially Modifiable Risk Factor for Neurochemical Brain Changes in Bipolar Disorders.Biological Psychiatry. 77(3): 295-303.
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8. Calkin C, Růžicková M, Uher R, Hajek T, Slaney CM, Garnham JS, O'Donovan MC, Alda M. (2015). Insulin resistance and outcome in bipolar disorder. British Journal of Psychiatry. 206(1): 52-57.
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Number of Contributors: 2
Description / Contribution Value: Invited manuscript. Early online DOI:10.1111/bdi.12330
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Description / Contribution Value: Invited manuscript

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Description / Contribution Value: Invited manuscript.
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Conference Publications

1. C. Calkin. *Insulin resistance takes center stage: a new paradigm in the progression of bipolar disorder*. Bipolar Disorders: An International Journal of Psychiatry and Neurosciences. International Society for Bipolar Disorders/ International Society for Affective Disorders, Amsterdam, Netherlands, Conference Date: 2016/7
Abstract
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Number of Contributors: 1
Description of Contribution Role: Single author hypothesis
2. Calkin C, Růžicková M, Uher R, Hajek T, Slaney C, Garnham J, O'Donovan C, Alda M. (2015). Comorbid insulin resistance may be an important factor in non-remitting bipolar disorder. Syllabus. Canadian Psychiatric Association annual meeting, Vancouver, Canada, Conference Date: 2015/10
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3. Calkin C, Růžicková M, Uher R, Hajek T, Slaney C, Garnham J, O'Donovan C, Alda M. (2015). Insulin resistance and outcome in bipolar disorder. Syllabus. Atlantic Provinces Psychiatric Association annual meeting, St. John's, Canada, Conference Date: 2015/6
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4. Calkin C. (2014). Insulin resistance: An occult, modifiable risk factor for refractory bipolar disorder. International Journal of Neuropsychopharmacology - supplement. 29th CINP World Congress of Neuropsychopharmacology, Vancouver, Canada, Vancouver, Canada (52-53), Conference Date: 2014/6
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Number of Contributors: 7
Funding Sources: NARSAD: Brain and Behavior Research Foundation - 18764
5. Calkin C. (2014). Co-morbid insulin resistance and type II diabetes predict chronic course of bipolar illness and poor response to lithium. Syllabus. American Psychiatric Association (APA) Annual Meeting, New York City, New York, New York City, United States, Conference Date: 2014/5
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Funding Sources: NARSAD: Brain and Behavior Research Foundation (USA) - 18764

6. Propper L, O'Donovan C, Růžicková M, Calkin C, Hajek T, Ortiz A, Slaney C, Garnham J, Alda M. (2013). Early-onset and very-early-onset bipolar disorder: Distinct or similar clinical conditions?. Syllabus. American College of Neuropsychopharmacology (ACNP), Hollywood, Florida, Hollywood, United States, Conference Date: 2013/12
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7. Calkin C, Růžicková M, Slaney C, Garnham J, Uher R, O'Donovan C, Alda M. (2013). Co-morbid insulin resistance and type II diabetes may predict poor response to lithium in patients with bipolar disorder. Syllabus. Dalhousie University Department of Psychiatry, Research Day, Halifax, Canada, Halifax, Canada, Conference Date: 2013/11
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8. Calkin C. (2013). Are comorbid insulin resistance and type II diabetes risk factors for refractory bipolar illness?. European Neuropsychopharmacology - supplement. European Congress of Neuropsychopharmacology, Barcelona, Spain, Barcelona, Spain (S366-S367), Conference Date: 2013/10
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Funding Sources: NARSAD: Brain and Behavior Research Foundation (USA) - 18764

9. Calkin C. (2012). The Risk and Burden of Insulin Resistance and Type 2 Diabetes in Bipolar Disorder. International Journal of Neuropsychopharmacology - supplement. International College of Neuro-Psychopharmacology (CINP) World Congress - Stockholm, Sweden, Stockholm, , Conference Date: 2012/6
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Funding Sources: Capital Health Research Fund (Canada) - 1003065

10. Calkin C, Van de Velde C, Růžicková M, Slaney C, Garnham J, Hajek T, O'Donovan C, Alda M. (2011). Can body mass index help predict prognosis and outcome in bipolar disorder?. Syllabus. 2011 World Congress of Biological Psychiatry (WFSBP) Annual Meeting, Prague, Czech Republic, Prague, Czech Republic, Conference Date: 2011/5
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11. Calkin C.(2010). Sub-phenotyping Bipolar Disorder as a Function of Diabetes Co-morbidity. Syllabus. Canadian Institute of Health Research: New Principal Investigators Meeting - Jackson's Point, Ontario, Canada, Jackson's Point, Canada,
Conference Date: 2010/7
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Funding Sources: Capital Health Research Fund - 1003065
12. Calkin C, Van de Velde C, Růžicková M, Slaney C, Garnham J, Hajek T, O'Donovan C, Alda M. (2009). Body mass index correlates of bipolar disorder: Can BMI help predict prognosis and outcome?. Syllabus. World Federation for the Society of Biological Psychiatry (WFSBP) Annual Meeting - Paris, France, Paris, France,
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13. Calkin C, Van de Velde C, Růžicková M, Slaney C, Garnham J, Hajek T, O'Donovan C, Alda M.(2009). Body mass index correlates of bipolar disorder: Can BMI help predict prognosis and outcome?. Syllabus. Society of Biological Psychiatry (SOBP), Vancouver, Canada, Vancouver, Canada,
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Conference Date: 2008/5
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Number of Contributors: 8