The University of Texas at Austin

# Institute for Mental Health Research

## Annual Report, FY 2016 – 2017

http://liberalarts.utexas.edu/imhr/index.php

The mission of the IMHR is to develop a novel, interdisciplinary, and high impact research program that incorporates scientific discoveries from neuroscience, computer science, and informatics into how psychosocial treatments are developed and delivered to patients, thereby substantially improving mental health for people residing in central Texas and beyond. Put simply, our ultimate goal is to provide patients with treatments that work when they are needed most and to deliver these treatments as quickly and effectively as possible.

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# Letter from the Director

August 31, 2017

This has been an exciting year at the Institute for Mental Health Research (IMHR). Arguably one of our most notable accomplishments was hiring a new tenure-track faculty member to join the IMHR, Dr. Kaya de Barbaro. We performed an extensive national search, reviewing over 100 applications and inviting four candidates for a multi-day interview. After this extensive search, Dr. de Barbaro was our top choice. Dr. de Barbaro's innovative research uses mobile sensing devices to monitor and measure the contributions of day-to-day experiences to mental health risks for mothers and their infants. This work is state-of-the-art and we feel fortunate to have recruited her to the IMHR and UT.

The IMHR also continued to expand its program of research. For instance, the Anxiety and Health Behavior Lab, led by Dr. Smits, recently started a research collaboration with the YMCA to examine the use of exercise to help smokers stop smoking. This is an especially exciting project, as it is testing whether an exercised-based smoking cessation program that was developed and tested in a research setting can also be effective when it is provided in a community settings. The Child Development in Context Lab, led by Dr. Neal-Beevers, is conducting an important longitudinal study to examine how social development unfolds over time in infants who have an older sibling without autism compared to infants with an older sibling with autism. Studies that involve the siblings of children with autism have the potential to reveal how and when social impairment in Autism develops, which should help identify the most critical periods for intervention. For a complete summary of currently funded research projects at the IMHR, please see the Grant Funding section on page 6.

Finally, the IMHR is providing important clinical services to the Austin community via the Anxiety and Stress clinic, which is supervised by Dr. Smits. The Anxiety and Stress Clinic is dedicated to providing high quality and affordable individual and group therapy for a variety of anxiety and stress-related disorders to the Austin community. Services are provided by faculty-supervised doctoral students in UT's highly ranked Clinical Psychology doctoral program and on a limited basis by licensed psychologists. Over the past year, the Anxiety and Stress Clinic provided more than 500 hours of clinical services to Austin residents. Given this success, we are actively developing new clinics, such as a Developmental Disorders clinic, so that we can provide state-of-the-art treatment to Austin residents.

Overall, this has been a terrific year for the IMHR. Thank you for your interest in our program and I hope you find this report to be useful. If you would like more information about the IMHR and our work, please feel free to contact me via email at beevers@utexas.edu or call me at 512-232-3706.

Sincerely,

Christopher Beevers, Ph.D.
Director, Institute for Mental Health Research
Professor and Wayne H. Holtzman Regents Chair in Psychology

# Background

Our aim is to develop a novel, interdisciplinary, and high impact research program that incorporates scientific discoveries from neuroscience, computer science, and informatics into how psychosocial treatments are developed and delivered to patients, thereby substantially improving mental health for people residing in central Texas and beyond. Put simply, our ultimate goal is to provide patients with treatments that work when they are needed most and to deliver these treatments as quickly and effectively as possible.

## AN URGENT NEED FOR BETTER MENTAL HEALTH TREATMENT

A 2015 report indicates that mental health conditions constitute the largest single source of world economic burden with an estimated global cost of $2.5 trillion. Indeed, 1 in 4 people will experience a mental health disorder at some point in their lives. Approximately 60 million US adults suffer from a diagnosable mental health condition and the World Health Organization estimates that 4 of the 10 leading causes of disability are mental health disorders. Closer to home, at least 11% of adult Texans suffer from serious mental health conditions costing the state billions of dollars due to expenses associated with treatment, lost productivity, and lost income. Unfortunately, *Texas ranks at or near the bottom in terms of per-capita mental health spending compared to other states*, placing our citizens at increased risk of poor outcomes. Improving psychosocial mental health treatment has tremendous potential to reduce suffering, disability, and economic burden on a very large scale.

## HOW SHOULD WE IMPROVE OUR MENTAL HEALTH TREATMENTS?

There is wide acceptance that efficient translation of basic science discoveries into clinical practice is critical for improving all forms of health care. Historically, in the 1950s and 1960s, basic and clinical research was largely conducted by scientists who also treated patients. However, over time, basic and clinical research developed into two distinct areas of research, with highly skilled and specialized researchers conducting basic science and clinicians primarily conducting clinical studies with patients. Additionally, clinicians who actually implement research gains into routine practice represent yet another separate but important group of individuals.

As a result, a translational gap has developed that limits communication and transfer of ideas among these research groups so that, in medicine, it takes an average of 17 years for discoveries in the laboratory to reach clinical practice. Alarmingly, the translation gap is even greater in psychiatry—it takes an average of 20 years from discovery to application! As just one example, there has been an explosion of neuroscience research related to mental health with virtually no application to treatment. *We believe that the Institute for Mental Health Research at The University of Texas at Austin can lead the world in translational research by developing new models of treatment development and implementation that reduce the lag time between discovery and application in the area of mental health treatment.*

## VISION FOR SUCCESS

Given the complexity of this problem, our approach to reducing the translation gap is multifaceted. We believe that the Institute for Mental Health Research has a unique opportunity to provide a higher level of care for our patients. We envision the further development of an interdisciplinary team that interacts seamlessly with researchers and clinicians in the Department of Psychology, Dell Medical School (including the Mulva Clinic for the Neurosciences), Computer Science, Engineering, Communications, and Data Science and Statistics (among others). There are three interrelated research efforts that would be critical for accelerating improvements in psychosocial treatments for mental health:

1. Building on existing work at the IMHR, we hope to continue to develop a multidisciplinary, intervention-related research group. Although there are number of directions this work could take us, we believe that harnessing the power of technological advances could be a significant boon to the development and dissemination of new treatments. This could include the development of internet-based interventions, a mobile sensing platform that detects symptom change, or a system that provides timely psychosocial interventions when they are needed most.

2. Another approach to enhancing the effectiveness of treatment is to provide patients with psychosocial treatments that have the greatest likelihood of being successful for that specific person. Precision medicine is at the heart of this effort, which aims to provide treatments tailored to the individual based on psychological, neural, genomic and behavioral information (broadly defined as biomarkers). Collaborating with faculty whose research focuses on the discovery, validation, and application of clinically-relevant biomarker research is an important step towards tailoring treatment to the individual rather than prescribing treatment in a trial-and-error fashion, as is the typical standard of practice.

3. Application of leading edge analytical methods will drive advances in translational research, particularly in regard to personalizing treatment. For instance, tremendous strides have been made in artificial intelligence, such as machine learning, for making personalized recommendations about the sorts of movies we would like or goods that we should buy. However, despite the obvious application to mental health, such methods are only very recently being applied to the problem of developing personalized mental health treatment recommendations. We believe that the IMHR is strongly positioned to lead this effort and help patients to obtain the treatments they need quickly and efficiently.

The IMHR focus of accelerating improvements in psychosocial treatment for mental health conditions is highly unique, as there are no other universities with research centers that have this focus. Thus, we think the IMHR is well positioned to rapidly become national leaders in mental health care in a way that is state-of-the-art, highly unique, and, most importantly, designed to provide significant relief to a large number of patients struggling with mental health conditions in central Texas and beyond. ***Providing financial support to the IMHR is critical to achieving these important goals.***

# IMHR Organizational Structure and Resources

The IMHR is an organized research unit within the College of Liberal Arts. It was established September 1, 2012 and is supported in part by the Judith M. Craig, Ph.D. Excellence Fund for Mental Health Research. The IMHR is a research institute that currently consists of four research laboratories:

- The Anxiety and Health Behaviors Lab, led by Jasper Smits, Ph.D. and Mark Powers, Ph.D., conducts state-of-the-art research aimed at improving the treatment of anxiety disorders and related problems.
- The Child Development in Context Lab, led by Rebecca Neal-Beevers, Ph.D., examines developmental processes that put children at risk for developmental disorders, such as autism and other related disorders.
- The Daily Activity Lab (website under development), led by Kaya de Barbaro, Ph.D., examines day-to-day activities and interactions between mothers and their infants in extended naturalistic home sessions (72 hours+) using a mobile sensor suite. The ultimate goal for this work is to access the basic mechanisms of early social-emotional development and to develop mobile interventions for cases of high risk, such as the transmission of risks for depression from mothers to infants.
- The goal of the Mood Disorders Laboratory, led by Christopher Beevers, Ph.D. and Jason Shumake, Ph.D., is to improve our understanding of the cognitive, biological, genetic, and environmental factors that cause and maintain depression and then use this knowledge to develop more effective treatments (i.e., translational research).

The IMHR is located in the Center for Liberal Arts (CLA) building. This space was selected because it is centrally located on campus, accessible and identifiable to research participants who are unfamiliar with campus. The IMHR includes approximately 7,000 square feet of dedicated space that includes research labs, a participant waiting room, a conference room, a computer lab for data processing and analysis, a biospecimen collection and storage room, office space for faculty, staff, post-doctoral fellows, and graduate students.

**Core IMHR Faculty (left to right)**: Christopher Beevers, Kaya de Barbaro, A. Rebecca Neal-Beevers, Mark Powers, Jason Shumake, Jasper Smits

Core IMHR faculty conduct research activities in laboratories located at the IMHR. As the IMHR mission is primarily research and clinical services, all faculty have appointments in departments where they conduct their teaching and service. All core faculty in the IMHR are affiliated with the Department of Psychology.

In addition to core faculty, there are a number of affiliated faculty with whom core faculty collaborate on various research projects. These affiliated faculty also make important contributions to the training of graduate students and post-doctoral fellows and are from a number of departments around the UT campus. Current affiliated faculty include: **Sarah Kate Bearman**, Ph.D. (Educational Psychology), **Yessenia Castro**, Ph.D. (Social Work), **Bharath Chandrasekaran**, Ph.D. (Communication Sciences and Disorders), **Jessica Church-Lang**, Ph.D. (Psychology), **Robert Josephs**, Ph.D. (Psychology), **Elizabeth Lippard**, Ph.D. (Psychiatry), **Marie Monfils**, Ph.D. (Psychology), **David Schnyer**, Ph.D. (Psychology), **Michael Telch**, Ph.D. (Psychology).

**Post-doctoral trainees**: The IMHR also includes a number of advanced trainees, such as post-doctoral fellows. Current post-doctoral fellows include Kean Hsu (Mood Disorders Lab) and Kimberley Ray (Mood Disorders Lab and the Cognitive Neuroscience Lab in the Department of Psychology led by Dr. Schnyer). Igor Marchetti was a visiting post-doctoral scholar from Belgium who trained with the Mood Disorders Lab from January to December, 2016.

**Graduate Students**: Training graduate students to become proficient clinical scientists is a central mission of the IMHR. Graduate students receive their training within the Clinical Psychology doctoral program in the Department of Psychology. Their research training (and some of their clinical training) occurs within the IMHR. Across the labs, approximately 10-15 doctoral students are trained within the IMHR each year. These students go on to have positions in universities, medical centers, and private practice.

**Full- and part-time time staff**: Full time staff generally coordinate ongoing studies and/or provide clinical treatment to study participants. The number of full time staff fluctuates depending on grant funding. Currently we have approximately 10 full or part-time staff at the IMHR. Many of these staff positions are filled by former students that have recently graduated and are obtaining additional research experience before applying to graduate school to obtain a Ph.D.

**Volunteer staff**: Another important mission at the IMHR is to provide undergraduate students with research experiences so they can obtain first-hand experience with the research process. For many students, these research experiences are crucial for helping them to determine whether they want to pursue a research focus in graduate school. Many of these students go on to graduate school and pursue their Ph.D. at other institutions around the country. Across all the labs, we have approximately 15-20 undergraduate students who volunteer in the IMHR every year.

# Grant Funding

Grants from the federal government and private foundations are a key source of funding for the IMHR. The table below lists the active grants awarded to core IMHR faculty. Despite a relatively bleak funding rate for federal research grants (whose budgets have been shrinking over the years), IMHR faculty have been quite successful obtaining funding. The grants listed below have IMHR faculty as principal investigators (PI). IMHR faculty often have other roles on grants, such as co-investigator and consultant. However, those grants are not included in this report for the sake of brevity and because those grants tend not to take place at the IMHR. See Appendix B for more detail about these studies.

## ACTIVE IMHR GRANTS

| PI | TITLE | DATES | SOURCE | AWARD |
|---|---|---|---|---|
| **Beevers** | *Genetic influences on dual processing modes of reward and punishment processing* | 4/01/12-1/30/18 | NIDA | $2,151,052 |
| **Beevers** | *Contribution of genome-wide variation to cognitive vulnerability to depression* | 09/16/16-08/31/18 | NIMH | $766,672 |
| **Beevers** | *Machine learning and personalized prognosis for depression treatment* | 07/01/16-05/31/19 | NIMH | $462,250 |
| **Beevers** | *Development of attention bias modification for depression* | 2/1/17-1/30/20 | NIMH | $1,754,833 |
| **Beevers** | *Perceptual and decisional processes underlying face perception biases in clinical depression* | Pending | NIMH | $420,557 |
| **de Barbaro** | *High-density markers of mother-infant bio-behavioral activity "in the wild": Developing a mobile-sensing paradigm to examine transmission of mental health* | 7/31/17 – 6/30/22 | NIMH | $591,760 |
| **Powers** | *Integrated PTSD and smoking treatment* | 7/3/13 – 6/30/18 | NIDA | $857,055 |
| **Powers** | *Virtual reality treatment in the medical setting: The societal burden of pain and opioid use* | 2016-2017 | UT | $100,000 |
| **Smits** | *Approach bias retaining to augment smoking cessation* | Pending | NIDA | $704,250 |
| **Smits** | *Dose timing of D-cycloserine to augment CBT for Social Anxiety Disorder* | 04/01/14-03/31/18 | NIMH | $695,250 |
| **Smits** | *Enhancing panic and smoking reduction treatment with D-cycloserine* | 09/15/13-08/31/18 | NIDA | $624,926 |
| **Smits** | *Exercise as an aid to smoking cessation in anxiety vulnerable adults* | 12/01/16-11/30/19 | CPRIT | $891,623 |
| | | | | $10,020,228 |

NIDA = National Institute on Drug Abuse; NIMH = National Institute for Mental Health; CPRIT = Cancer Prevention & Research Institute of Texas

# Publications and Other Scholarly Output

One of the key ways in which the IMHR disseminates its research findings is through scientific publications. In the past three years, IMHR faculty and trainees have published **65** peer-reviewed journal articles, made numerous presentations at national and international conferences, and conducted workshops both locally and for national and international organizations. This represents a remarkable level of scientific productivity. A full list of recent peer-reviewed publications since Jan 1, 2015 is included in Appendix A. Below are a few selected examples of recent publications, presentations, and workshops:

## HIGHLIGHTED PUBLICATIONS

*denotes IMHR trainee

**Beevers, C.G.**, *Pearson, R., *Hoffman, J., *Foulser, A.A., Shumake, J., & Meyer, B. (2017). Effectiveness of an Internet intervention (Deprexis) for depression in an US adult sample: A parallel-group pragmatic randomized controlled trial. *Journal of Consulting and Clinical Psychology, 85, 367-380.*

*Pearson, R., Palmer, R.C., Brick, L.A., McGeary, J.E., Knopik, V.S., **Beevers, C.G**. (2016). Additive genetic contribution to symptom dimensions in Major Depressive Disorder. *Journal of Abnormal Psychology, 125,* 495-501.

**Smits, J. A. J.**, Zvolensky, M. J., *Davis, M. L., Rosenfield, D., Marcus, B. H., Church, T. S., Powers, M. B., Frierson, G. M., Otto, M. W., *Hopkins, L. B., & *Baird, S. O. (2016). The efficacy of vigorous-intensity exercise as an aid to smoking cessation in adults with high anxiety sensitivity: A randomized controlled trial. *Psychosomatic Medicine, 78*, 354-364.

*Jacquart, J., Roquet, R. F., **Powers, M. B.**, *Papini, S., Rosenfield, D., **Smits, J. A. J.**, & Monfils, M. H. (2017). Effects of acute exercise on fear extinction in rats and exposure therapy in humans: Null findings from five experiments. *Journal of Anxiety Disorders, 50*, 76-86.

## HIGHLIGHTED PRESENTATIONS

***Jacquart, J.** *An exercise augmented smoking cessation treatment for individuals with high anxiety sensitivity: The relationship between attendance patterns and quit success.* Presented at the International Society of Sport Psychology World Congress, Seville, Spain

**Beevers, C.G.** *Predictors of treatment response to an internet intervention for depression.* Berlin, Germany. Annual meeting of the World Psychiatric Association (October, 2017).

*Dowd, A.C., *Davidson, A.C., & **Neal-Beevers, A.R.**, (2017, April). *Social responsiveness at 12 and 15 months predicts severity of social deficits at 4-Years in infant siblings*. Presented at the International Meeting for Autism Research, San Francisco, CA.

## HIGHLIGHTED WORKSHOPS

**Smits, J.A.J.** Behavioural Science Institute of Radboud Universiteit (June, 2016). Exposure therapy: new augmentation procedures & expert skills training. Invited lecture/workshop. Nijmegen, The Netherlands.

**Smits, J.A.J.** American Psychological Association (April, 2017). Exercise for mood and anxiety disorders. Webinar.

**Power, M.B.** Prolonged Exposure Therapy Workshops: University of Regina, Canada; Radboud University, The Netherlands; UT Austin; Baylor University Medical Center

# Collaboration with Industry

Industry partners reach out to IMHR faculty (or vice versa) to develop research studies and test innovative products or ideas that would not be possible without assistance from industry. This often means that IMHR research is involved in the development of state-of-the-art technologies or scientific approaches that are in the early stages of research and development. A few recent examples of collaboration with industry include:

**Virtual Reality Treatment in the Medical Setting: Reducing the Societal Burden of Pain and Opioid Use**

Principal Investigator: Mark Powers, Ph.D.

Funded by a $100,000 seed money from the LIFT program at UT, Dr. Powers collaborated with an Austin-based company developing virtual reality (VR) technologies that could be used to develop new innovative treatments. Specifically, recent advances in VR technology (i.e., improved realism and immersion using 360-degree 3D technology and more affordable delivery systems) allow the development of more realistic and more cost-effective applications. Capitalizing on these advances and our experiences with VR intervention development and evaluation, we will create and test a state-of-the-art VR experience and compare it to established standard animated VR content for pain management in a medical setting.

**Internet Intervention for Depression**

Principal Investigator: Christopher Beevers, Ph.D. and Jason Shumake, Ph.D.

Drs. Beevers and Shumake have been collaborating over the past several years with a German company, GAIA, on the development of an Internet Intervention designed to treat depression in adults. GAIA is a global pioneer in digital therapy, launching its first program successfully in 2001, that develops therapeutic software for physicians, therapists, payers and patients. Together with GAIA, Drs. Beevers and Shumake have conducted several clinical trials of Deprexis and are now using machine learning methods to predict who is most likely to respond to this treatment.

**Cloud computing and mental health research**

Principal Investigator: Jason Shumake, Ph.D.

Dr. Shumake has been collaborating with an Austin-based company, Cloudera, to use state-of-the-art data analytic tools in a cloud computing environment. Couldera is providing access their suite of analysis tools so that we are able to analyze big data (e.g., contribution of variation in human genome to treatment response) and identify novel insights that otherwise would not be possible.

# Trainee Outcomes

An important aspect of the work at the IMHR is to help trainees at all levels receive exposure to the research process and develop their research competence and skills. As a result, we have placed a number of research assistants and graduate students in research and clinical positions around the country. Several recent outcomes include:

- **Justin Dainer-Best**, a doctoral student supervised by Dr. Beevers, is completing his internship at the University of Vermont
- **Michele Davis**, a doctoral student supervised by Dr. Smits, is completing her internship at the Baylor College of Medicine at the Menninger Department of Psychiatry and Human Behavior.
- **Bridget Gamber Davidson**, a doctoral student supervised by Dr. Neal-Beevers, accepted a faculty position at the Mailman Center for Child Development in the Department of Pediatrics at the University of Miami Miler School of Medicine.
- **Johnna Medina, Ph.D.**, a doctoral student supervised by Dr. Smits, accepted a post-doctoral positon at the Stanford University School of Medicine
- **Peter Clasen, Ph.D.**, a doctoral student supervised by Dr. Beevers, accepted a position as a user experience researcher at Facebook.
- **Alban Foulser**, a post-baccalaureate lab manager in Dr. Beevers lab, was accepted into the doctoral program in clinical psychology at the University of Texas at Austin.
- **Daniel Ikejimba**, an undergraduate supervised by Dr. Neal-Beevers, was accepted into a doctoral program in clinical psychology at the University of Hawaii.
- **Saba Masood**, an undergraduate supervised by Dr. Neal-Beevers, was accepted into a doctoral program in clinical psychology at the University of Texas Southwestern Dallas Medical School.

# Service to Community

The IMHR research and clinical services provide an important avenue for engagement with the Austin community. We provide educational opportunities and direct clinical services to the Austin community.

- The IMHR provides established, evidence-based treatments to the community via its associated clinics. Over time we expect to develop a series of clinics that focus on treatment for a number of mental health conditions. The Anxiety & Stress Clinic at the IMHR is dedicated to providing high quality and affordable individual and group therapy for a variety of anxiety and stress-related disorders to the Austin community. Treatment services are designed to provide effective psychological care in a compassionate environment to members of the University of Texas at Austin (UT) campus and general public. Services are provided by faculty-supervised doctoral students in UT's highly ranked Clinical Psychology doctoral program and on a limited basis by licensed psychologists. The clinic is affiliated with the Anxiety and Health Behaviors Laboratory at the Institute for Mental Health Research.

# Other Service Activities and Accomplishments

The faculty provide service to the scientific community at a variety of different levels, including service to the university, college, national and international organizations. This includes committee work for the department and college, reviewing research papers for scientific journals, editorial activities for journals, reviewing grants for federal and international funding agencies, and beyond. In addition, IMHR faculty and students have received a number of notable awards and recognitions.

## SELECTED SERVICE ACTIVITIES

- Dr. Beevers served as a grant reviewer for the Research Foundation - Flanders (Fonds Wetenschappelijk Onderzoek - Vlaanderen, FWO) and for the National Institute of Mental Health, Experimental Therapeutics Clinical Trials study section.
- Dr. Beevers participated in The Texas Edge event in Dallas, TX, sponsored by UT Alumni Association, and was part of a panel discussion on the topic of mental health research.
- Dr. Smits participated in The Texas Edge event in Midland, TX, sponsored by UT Alumni Association, and was part of a panel discussion on technology and health care
- Dr. Smits, Powers, and Beevers are members of the Scientific Advisory Board for the Anxiety and Depression Association of America (ADAA)
- Dr. Smits is an Associate Editor for three journals: *Journal of Consulting and Clinical Psychology*, *Journal of Anxiety Disorders*, and *Cognitive Therapy and Research*
- Dr. Beevers accepted a position as Associate Editor of Clinical Psychological Science
- Dr. Smits served as chair for the American Psychological Association, Division 12 Annual Conference
- Dr. Neal-Beevers reviews conference submissions for International Meeting for Autism Research
- Dr. Powers was Chair of the APA Division 12 Presidential Task Force on Empirically Supported Treatment Dissemination
- Dr. Powers is the Editor-in-Chief of the journal *Cognitive Behaviour Therapy*

## SELECTED HONORS

- Dr. Beevers received the Distinguished Alumni Award, Department of Psychology, University of Miami.
- Dr. Beevers became a Fellow of the Association for Psychological Science

# Appendix A: IMHR Publications past 3 years

1. Lindner P, Miloff A, Hamilton W, Reuterskiold L, Andersson G, Powers MB, et al. Creating state of the art, next-generation Virtual Reality exposure therapies for anxiety disorders using consumer hardware platforms: design considerations and future directions. Cogn Behav Ther. 2017 Sep;46(5):404–20.

2. McLaughlin C, Kearns NT, Bennett M, Roden-Foreman JW, Roden-Foreman K, Rainey EE, et al. Alcohol and drug toxicology screens at time of hospitalization do not predict PTSD or depression after traumatic injury. Am J Surg. 2017 Sep;214(3):390–6.

3. Jacquart J, Roquet RF, Papini S, Powers MB, Rosenfield D, Smits JAJ, et al. Effects of acute exercise on fear extinction in rats and exposure therapy in humans: Null findings from five experiments. J Anxiety Disord. 2017 Aug;50:76–86.

4. Zvolensky MJ, Bakhshaie J, Norton PJ, Smits JAJ, Buckner JD, Garey L, et al. Visceral sensitivity, anxiety, and smoking among treatment-seeking smokers. Addictive Behaviors. 2017 Jun;75:1–6.

5. Kearns NT, Blumenthal H, Rainey EE, Bennett MM, Powers MB, Foreman ML, et al. Discrepancy in caregiving expectations predicts problematic alcohol use among caregivers of trauma injury patients six months after ICU admission. Psychol Addict Behav. 2017 Jun;31(4):497–505.

6. Schnyer DM, Clasen PC, Gonzalez C, Beevers CG. Evaluating the diagnostic utility of applying a machine learning algorithm to diffusion tensor MRI measures in individuals with major depressive disorder. Psychiatry Res. 2017 Jun;264:1–9.

7. Disner SG, Shumake JD, Beevers CG. Self-referential schemas and attentional bias predict severity and naturalistic course of depression symptoms. Cogn Emot. 2017 Jun;31(4):632–44.

8. Mataix-Cols D, Fernandez de la Cruz L, Monzani B, Rosenfield D, Andersson E, Perez-Vigil A, et al. D-Cycloserine Augmentation of Exposure-Based Cognitive Behavior Therapy for Anxiety, Obsessive-Compulsive, and Posttraumatic Stress Disorders: A Systematic Review and Meta-analysis of Individual Participant Data. JAMA Psychiatry. 2017 May;74(5):501–10.

9. Jacquart J, Papini S, Davis ML, Rosenfield D, Powers MB, Frierson GM, et al. Identifying attendance patterns in a smoking cessation treatment and their relationships with quit success. Drug and alcohol dependence. 2017 May;174:65–9.

10. Sullivan E, Shelley J, Rainey E, Bennett M, Prajapati P, Powers MB, et al. The association between posttraumatic stress symptoms, depression, and length of hospital stay following traumatic injury. Gen Hosp Psychiatry. 2017 May;46:49–54.

11. Roden-Foreman JW, Bennett MM, Rainey EE, Garrett JS, Powers MB, Warren AM. Secondary traumatic stress in emergency medicine clinicians. Cogn Behav Ther. 2017 Apr;:1–11.

12. Beevers CG, Pearson R, Hoffman JS, Foulser AA, Shumake J, Meyer B. Effectiveness of an internet intervention (Deprexis) for depression in a united states adult sample: A parallel-group pragmatic randomized controlled trial. J Consult Clin Psychol. 2017 Apr;85(4):367–80.

13. Porter RJ, Hammar A, Beevers CG, Bowie CR, Nodtvedt OO, Peckham AD, et al. Cognitive and affective remediation training for mood disorders. Aust N Z J Psychiatry. 2017 Apr;51(4):317–9.

14. Maddox WT, Gorlick MA, Koslov S, Mcgeary JE, Knopik VS, Beevers CG. Serotonin Transporter Genetic Variation is Differentially Associated with Reflexive- and Reflective-Optimal Learning. Cerebral Cortex. 2017 Feb;27(2):1182–92.

15. Curtiss J, Andrews L, Davis M, Smits J, Hofmann SG. A meta-analysis of pharmacotherapy for social anxiety disorder: an examination of efficacy, moderators, and mediators. Expert Opin Pharmacother. 2017 Feb;18(3):243–51.

16. Palmer RHC, Beevers CG, Mcgeary JE, Brick LA, Knopik VS. A Preliminary Study of Genetic Variation in the Dopaminergic and Serotonergic Systems and Genome-wide Additive Genetic Effects on Depression Severity and Treatment Response. Clin Psychol Sci. 2017 Jan;5(1):158–65.

17. Papini S, Ruglass LM, Lopez-Castro T, Powers MB, Smits JAJ, Hien DA. Chronic cannabis use is associated with impaired fear extinction in humans. J Abnorm Psychol. 2017 Jan;126(1):117–24.

18. Hearon BA, Beard C, Kopeski LM, Smits JAJ, Otto MW, Bjorgvinsson T. Attending to Timely Contingencies: Promoting Physical Activity Uptake Among Adults with Serious Mental Illness with an Exercise-For-Mood vs. an Exercise-For-Fitness Prescription. Behav Med. 2016 Dec;:1–8.

19. Baldwin AS, Kangas JL, Denman DC, Smits JAJ, Yamada T, Otto MW. Cardiorespiratory fitness moderates the effect of an affect-guided physical activity prescription: a pilot randomized controlled trial. Cogn Behav Ther. 2016 Nov;45(6):445–57.

20. Salley B, Sheinkopf SJ, Neal-Beevers AR, Tenenbaum EJ, Miller-Loncar CL, Tronick E, et al. Infants' early visual attention and social engagement as developmental precursors to joint attention. Developmental Psychology. 2016 Nov;52(11):1721–31.

21. Otto MW, Eastman A, Lo S, Hearon BA, Bickel WK, Zvolensky M, et al. Anxiety sensitivity and working memory capacity: Risk factors and targets for health behavior promotion. Clin Psychol Rev. 2016 Nov;49:67–78.

22. Foa EB, McLean CP, Zang Y, Zhong J, Rauch S, Porter K, et al. Psychometric properties of the Posttraumatic Stress Disorder Symptom Scale Interview for DSM-5 (PSSI-5). Psychol Assess. 2016 Oct;28(10):1159–65.

23. Foa EB, McLean CP, Zang Y, Zhong J, Powers MB, Kauffman BY, et al. Psychometric properties of the Posttraumatic Diagnostic Scale for DSM-5 (PDS-5). Psychol Assess. 2016 Oct;28(10):1166–71.

24. Ellis AJ, Shumake J, Beevers CG. The effects of respiratory sinus arrhythmia on anger reactivity and persistence in major depression. Psychophysiology. 2016 Oct;53(10):1587–99.

25. Davis ML, Rosenfield D, Bernstein A, Zvielli A, Reinecke A, Beevers CG, et al. Attention bias dynamics and symptom severity during and following CBT for social anxiety disorder. J Consult Clin Psychol. 2016 Sep;84(9):795–802.

26. Disner SG, Beevers CG, Gonzalez-Lima F. Transcranial Laser Stimulation as Neuroenhancement for Attention Bias Modification in Adults with Elevated Depression Symptoms. Brain Stimulation. 2016 Sep;9(5):780–7.

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# Appendix B: Active IMHR grants

**Title**: Genetic influences on dual processing modes of reward and punishment learning
**PI**: Christopher Beevers (co-I: John McGeary and Valerie Knopik, Brown University)
**Dates**: 1-APR-2012 to 31-JAN-2018
**Source**: National Institute on Drug Abuse
**Total costs**: $2,151,052
**Description**: Deficiencies in reward and punishment processing are theoretical cornerstones of alcohol and substance dependence, addiction, and other psychopathology. However, most research ignores the fact that contemporary cognitive theory emphasizes two processing modes: a reflective mode where processing is under conscious control and predominantly frontally-mediated, and a reflexive mode that is not under conscious control and is predominantly striatally-mediated. In addition, a detailed understanding of the genetic underpinnings of dual processing modes of reward and punishment is critical to improving our theories of addiction and psychopathology and to translational work focused on developing interventions. Dopamine and serotonin genes are hypothesized to affect reflexive and reflective reward and punishment processing and are therefore the focus of this proposal. The overall goal of this project is to test specific hypotheses regarding dopaminergic and serotonergic genetic variation on reflexive and reflective reward and punishment processing. We use classification learning tasks for which the optimal mode of processing (reflective or reflexive) can be defined rigorously and for which the research team has over 20 years of experience. The proposed studies will also complement a single nucleotide polymorphism approach with a haplotype strategy, which will determine whether additional variants in these dopaminergic and serotonergic genes also influence reward and punishment processing. We will also account for population stratification by testing and statistically controlling for occult population substructure. Aim 1 examines associations between genetic variation in dopaminergic and serotonergic systems with reward and punishment processing when optimal performance is mediated by the reflexive system or by the reflective system. Aim 2 examines the effects of "reflexive system" genetic variation on reflective-optimal task performance, and "reflective system" genetic variation on reflexive-optimal task performance. Aim 3 examines the influence of stress on reflexive reward and punishment processing. The proposed studies are the first to attempt to characterize the interactive effects of serotonin, dopamine and stress on cognitive processing of rewards and punishment using contemporary cognitive frameworks. This integrative, interdisciplinary research approach will provide the critical foundation needed for future translational work that examines how these processes go awry in clinical disorders.

**Title**: Contribution of genome-wide variation to cognitive vulnerability to depression
**PI**: Christopher Beevers (other PIs: John McGeary, Brown University; John Allen, University of Arizona)
**Dates**: 16-SEP-2016 to 31-AUG-2018
**Source**: National Institute of Mental Health
**Total costs**: $766,672
**Description**: Depression is a leading cause of disability worldwide among adults. Cognitive models of depression, which have received strong empirical support, posit that individuals' characteristic ways of

attending to, interpreting, and remembering stimuli in their environment may contribute to the development and maintenance of the disorder. To understand the etiology of these biases, many genetic association studies have been completed. However, findings so far (including those from our own work) have been somewhat limited. Although genetic association studies have value, we strongly believe that whole genome methods will provide new insights into the role of genetic variation in psychopathology. Aim 1 is to comprehensively measure phenotypes related to negative cognitive bias in a community sample of 1500 adults of European ancestry. We propose to use established behavioral, eye tracking, and electrophysiological tasks to comprehensively measure negatively biased attention, interpretation, and memory—central features of contemporary cognitive models of depression. Aim 2 is to quantify the aggregate contribution of genetic variation across the genome to cognitive vulnerability. We propose to use genomic-relatedness-matrix restricted maximum likelihood to estimate the aggregate genetic effect of approximately 900,000 polymorphisms that measure exomic and common genetic variation across the entire genome. This will provide an answer to the fundamental question of how much variance in these key phenotypes is due to variation in measured polymorphisms. Aim 3 is to develop biologically plausible cumulative genetic scores (CGS) to identify linkages between specific genetic variation and our phenotypes. We have created gene sets derived from a database of known and predicted protein interactions and from human brain atlases with genetic and anatomic information. Importantly, our large sample allows us to perform a confirmatory study for these gene sets. Upon study conclusion, we will make our data publically available so investigators can develop additional gene sets that putatively relate to cognitive vulnerability. In sum, the proposed study will provide much needed insight into the degree to which these theoretically motivated intermediate phenotypes for depression are associated with genetic variation. Although twin studies point to the possibility of a genetic etiology, no attempts have been made to quantify the contribution of measured genetic variation to these cognitive phenotypes. This will provide much needed guidance about how much variance in cognitive vulnerability to depression can be predicted with genome- wide based analyses and may help account for some of the missing heritability often associated with candidate polymorphism studies.

**Title**: Machine Learning and personalized prognosis for depression treatment
**PI**: Beevers, Christopher (co-I: Shumake, Jason)
**Dates**: 1-JUL-2016 to 31-MAY-2019
**Source**: National Institute of Mental Health
**Total costs**: $462,250
**Description**: Depression treatment is effective for approximately 50-60% of patients who receive treatment, but the probability of a successful response is typically unknown before treatment begins. As a result, depression treatment is routinely delivered in a trial-and-error fashion until a satisfactory response is achieved. Our objective is to provide a personalized prognosis by applying ensemble machine learning techniques to discover novel, non-linear combinations of multiple weak predictors that collectively yield accurate predictions of treatment outcome. This statistical approach considers many prediction variables simultaneously and iteratively constructs a complex prediction model that often dramatically outperforms traditional statistical methods. Aim 1 is to apply stochastic gradient boosted decision trees to predict response to citalopram using archival data from the STAR*D clinical trial. In preliminary analyses, we randomly selected 1223 patients to train the model and another 407 patients to independently test the model (a 75-25 split),

with tuning parameters selected by cross-validation to minimize log-loss. The resulting prediction on the independent test sample was superior to the no-information rate ($p < 0.001$), with an overall predictive accuracy of 66%. Although this level of prediction is significantly better than a no information model, we plan to improve the model's prognostication by 1) adding features that capture the "pharmacological noise" of concurrent (non- study) medication use and 2) updating model predictions based on early signs of response. Aim 2 is to use a similar machine learning approach to examine response to internet-based CBT for depression. Internet-based treatments for depression are growing in popularity, provide efficient access to health care, reduce treatment costs, and have good evidence for treatment efficacy. Importantly, we have a large dataset (N = 1,013) within which to develop treatment-matching algorithms that predict treatment response based on patient attributes. Study Impact: The overarching goal of this project is to use machine learning methods to develop treatment matching algorithms. In the long term, we can envision a system that evaluates a patient on a number of important predictor variables and provides a personalized probability of treatment success. These probabilities would then be used to guide treatment selection or modify current treatment if a poor response is predicted. Developing algorithms that successfully predict whether a particular form of treatment is likely to be successful for a patient with a given set of attributes would be a tremendous step towards efficient and personalized depression treatment.

**Title**: Development of attention bias modification for depression
**PI**: Beevers, Christopher (co-PI: David Schnyer; Co-Is: Jason Shumake, Jasper Smits)
**Dates**: 1-FEB-2017 to 31-JAN-2020
**Source**: National Institute of Mental Health
**Total costs**: $1,754,833
**Description**: The overall goal of this project is to continue development of an attention bias modification (ABM) intervention that targets and reduces negative attention bias among adults with elevated symptoms of depression. Our prior work indicates that attention bias for negative information is associated with the maintenance of depression and that neural circuitry within frontal-parietal brain networks supports biased attention for negative information, thus allowing us to develop specific and targeted interventions that directly alter the neurobiology of negative attention bias. The proposed R33 study builds upon our prior NIMH funded work (R21MH092430), which examined whether ABM reduces negative attention bias and improves symptoms of depression. Findings indicate that compared to placebo ABM, active ABM reduced negative attention bias and increased resting state connectivity within a neural circuit (i.e., middle frontal gyrus and dorsal anterior cingulate cortex) that supports control over emotional information. Further, change in negative attention bias from pre- to post-ABM was significantly correlated with depression symptom change but only in the active training condition. Importantly, a 40% decrease in symptoms was observed in the active training condition; however, similar symptom reduction was also observed in the "placebo ABM" condition. Exploratory analyses indicated that placebo training may have promoted depression improvement by enhancing sustained attention. Although these preliminary findings are encouraging and demonstrate that ABM successfully alters the treatment target (i.e., negative attention bias), our prior work is among the first to document efficacy of ABM among adults with clinically significant depression. We believe it is prudent and necessary to obtain additional efficacy evidence for ABM before moving forward with large-scale clinical trials of ABM for depression. Aim 1 is to conduct a randomized clinical trial among adults with elevated symptoms

of depression and a negative attention bias that compares the efficacy of active ABM to placebo ABM and an assessment-only control condition that does not involve any ABM procedures. Aim 2 is to examine whether ABM alters negative attention bias and functional connectivity within frontal-parietal neural circuitry that support negative attention bias. Aim 3 is to identify mechanisms responsible for the putative efficacy of active and placebo ABM. Study Impact: The current project proposes to target and reduce negative attention bias with a novel intervention grounded in basic psychopathology research. We believe this experimental medicine approach will lead to the development of a highly specific and targeted intervention, using cutting- edge cognitive neuroscience to inform treatment development, and improve the quality of life of people whose psychopathology is maintained by negative attention bias.

**Title**: Perceptual and decisional processes underlying face perception biases in clinical depression
**PI**: Christopher Beevers (co-PI: Fabian Soto, Florida International University)
**Dates**: 1-JAN-2018 to 31-DEC-2019 (pending award notice)
**Source**: National Institute of Mental Health
**Total costs**: $420,557
**Description**: Cognitive models of depression suggest that the development and maintenance of this disorder stem from individuals' characteristic ways of attending to, interpreting, and remembering environmental stimuli, such as selective attention toward negative aspects of experience. In face perception, these biases are expressed as a tendency to interpret ambiguous faces as expressing negative emotion and a general impairment in processing of emotional faces. Our pilot research with dysphoric participants also suggests that the ability to process other important face dimensions (e.g., identity) independently from emotion might be impaired in depression, but research on this aspect of face perception in clinical depression has been very limited. Obtaining a better understanding of all these face perception impairments is critical, as the ability to correctly extract information from faces is important for adequate social interaction. Social impairments observed in depression could be produced or intensified by face perception impairments. The impairments in face processing observed in depression could be due to to early, perceptual processes (i.e., people with depression perceive emotional expression differently), or they could be due to late, decisional processes (i.e., people with depression interpret emotional expression differently). This distinction is important, as some treatments for depression are able to target only one of these two levels. This project proposes to use state-ˇof-ˇthe-ˇart computational and psychophysical approaches to identify the precise locus of the impairments in face emotion processing in depression. More specifically, we will use recent advances in general recognition theory (to which we have contributed) and in classification images techniques, to study whether the ability to process face emotion and identity in a relatively independent fashion is altered in depression. Our approach will allow us to additionally test whether biases in emotion identification previously observed in depression are due to perceptual or decisional processes. Finally, our previous research shows that categorization training can improve both discriminability and independence of novel face dimensions, and these effects were observed at both the perceptual and decisional levels. An exploratory goal of this project is to test whether training depressive patients in an emotion categorization task might also reduce both perceptual and decisional biases in face perception.

**Title**: High-density markers of mother-infant bio-behavioral activity "in the wild": Developing a mobile-sensing paradigm to examine transmission of mental health risks
**PI**: Kaya de Barbaro
**Dates**: 16-AUG-2017 to 31-JUL-2021
**Source**: National Institute of Mental Health
**Total costs**: $591,760
**Description**: Major theories of socioemotional development suggest that adaptive patterns of self-regulation reflect the accumulation of thousands of individual daily experiences of distress. In particular, parents' efforts to regulate their infants' distress are thought to provide critical inputs to developing self-regulation skills. Factors affecting caregiving, such as caregiver stress or mood disorders, are thought to limit parents' ability to provide this early support. Thus, early-emerging patterns of mother-infant interaction are theorized to be an important mechanism by which mental health risks are transmitted from caregivers to their children. However, empirical evidence for these theories are scarce, as it has not been possible to systematically capture episodes of distress as they occur in day-to-day mother and infant activity. Additionally, most studies cannot disentangle complex interactions between infant and maternal psychobiological factors. For example, highly fussy infants are more likely to stress and overwhelm their parents, thereby likely affecting parental regulation efforts and potentially exacerbating their own early biological predispositions. Datasets capturing the details of daily interactions between mothers and their infants are needed to access the basic bio-behavioral mechanisms of developing psychopathology risk. In the future, such rich datasets could also provide a foundation for emerging "just in time" interventions that could provide mothers with real-time support and reassurance during day-to-day activities. To thus advance the field of developmental psychopathology, this proposal will leverage emerging "wearable" or mobile-sensor technologies to capture episodes of infant distress and subsequent maternal regulation efforts as they occur in the typical day-to-day activities of infants and their mothers. The research aims of this proposal are 1) to develop a mobile-sensing platform that will automatically detect detailed markers of mother-infant distress-related activity as participants go about their daily lives, captured via a synchronized suite of "wearable" physiology, audio and proximity sensors, and once validated, to use this platform to 2) investigate the daily mechanisms of maladaptive mother-infant interaction dynamics The training goals of this proposal are to 1) develop my expertise with state-of-the art computational tools to study mother-infant activity in the "wild", allowing me unprecedented access to the dynamic processes of bio- behavioral development, and 2) to provide me the opportunity bridge my work to the domain of developmental psychopathology. The proposed K01 is thus a key step in my goal to develop a research program that can harness the rich dynamics of day-to-day activity to support theoretically-driven clinical innovations.

**Title**: Integrated PTSD and smoking treatment
**PI**: Mark Powers
**Dates**: 3-JUL-2013 to 30-JUN-2018
**Source**: National Institute on Drug Abuse
**Total costs**: $857,065
**Description**: My primary research interests center around developing efficacious and effective behavioral interventions for substance use problems among adults with post-traumatic stress disorder (PTSD). Here, my

clinical and research experiences have guided me to focus on smoking cessation. Clinically, I have observed that smoking is prevalent among patients who present for the treatment of PTSD, and that anxiety processes often serve to smoking. A growing body of research supports these observations. Moreover, extant smoking cessation interventions have often failed to yield lasting clinical change. These observations converge with one another to suggest that there is scientific and clinical merit to developing interventions that target anxiety processes and PTSD in one overarching model. My research experience to date is primarily in the area of the nature, causes, and treatment of anxiety disorders. Thus, my proposed line of research requires further training in substance use disorders. In the short- term, my professional goals provide clear direction for further training. would like to use the K01 mechanism to build upon my previous experience and training in three meaningful ways. First, I selected two mentors [Drs. Smits (Primary) and Zvolensky (Co-Mentor)] who can guide me in my efforts to develop an independent research program focusing on smoking cessation. Dr. Smits and Zvolensky bring expertise in the development and evaluation of interventions for anxiety and related substance use problems. Second, with help of Dr. Foa, an internationally-recognized expert in PTSD, I have developed a curriculum to build my expertise in PTSD. Third, I have planned a series of courses and meetings with Dr. Rosenfield, a biostatistician, to learn about statistical methods as it relates to testing mediatio and moderation. Together, these integrated training experiences will help me reach my long-term goal, which is to pursue this independent line of work as a tenured faculty member in a psychology department. The research plan of this K01 application is consistent with my transition to substance use disorder research. This K01 research plan aims to develop and test an integrated intervention for improving the outcome of cognitive-behavioral therapy (CBT) for smoking cessation in adults with PTSD. PTSD is associated with increased smoking and failed cessation attempts.2-7 The prevalence of smoking in persons with PTSD is 44.6 %, compared to 22.5% in persons with no psychiatric disorder.8 Smokers with PTSD are more likely to be dependent,4 smoke heavily (> 25 cigarettes per day),2 experience more severe withdrawal symptoms, and relapse following a quit attempt.2 In fact, the quit rate in smokers with PTSD (23.2%) is one of the lowest of all mental disorders.8Thus, the vast majority of persons with PTSD attempting to quit smoking do not benefit from existing intervention protocols. Clearly, there is a need for the development of specialized or personalized strategies for this population. Features of PTSD that may contribute to smokers' progression to nicotine dependence and cessation relapse include negative affect, fear, increased arousal, irritability, anger, distress intolerance, and anxiety sensitivity. Anxiety sensitivity is higher in persons with PTSD than in any other anxiety disorder except for panic disorder.9 High anxiety sensitivity is uniquely associated with greater odds of lapse10 and relapse11-13 during quit attempts.13 Distress intolerance, a perceived or behavioral tendency to not tolerate distress,14 is related to both the maintenance of PTSD and problems in quitting smoking.15 Fear extinction-based treatments (i.e., prolonged exposure [PE], interoceptive exposure [IE]) have shown efficacy for reducing PTSD16 and distress intolerance and anxiety sensitivity17-19 and therefore emerge as promising candidates to augment standard smoking cessation interventions for individuals with PTSD. The present application proposes to pilot test an integrated and specialized treatment for smokers with PTSD. This Integrated PTSD and Smoking Treatment (IPST) combines cognitive-behavioral therapy and nicotine replacement treatment for smoking cessation (standard care; SC) with PE to target PTSD symptoms (e.g., negative affect, fear, increased arousal, irritability, anger) and IE to reduce anxiety sensitivity and distress intolerance. To thi end, 80 adult smokers with PTSD will be randomly assigned to either: (1) IPST or (2) SC.

Smoking outcomes will be assessed 2, 4, 8, 10, 16, and 24 weeks after quit date. Measure of putative mediators will be assessed repeatedly prior and following the quit date.

**Title**: Enhancing panic and smoking reduction treatment with D-cycloserine.
**PI**: Jasper Smits (co-PIs: Michael Otto, Boston University; Michael Zvolensky, University of Houston)
**Dates**: 15-SEP-2013 to 31-AUG-2018
**Source**: National Institute on Drug Abuse
**Total costs**: $624,926
**Description**: Approximately 9-15 million smokers in the U.S. meet criteria for at least one anxiety disorder during their lifetime (Kessler et al., 2005) and these persons experience significant challenges quitting tobacco (Piper et al., 2010a; Zvolensky et al., 2008). Yet, little attention has been given to the maintenance of tobacco use among persons with anxiety disorders, and in particular, smokers with a history of panic attacks. This group is especially important to study because research shows that they have significantly lower quit rates than smokers with no history of panic attacks, and that they respond the same to placebo, single cessation, and combination cessation pharmacotherapy (Piper et al., 2010a). The goal of the current research is to pilot test the efficacy of the addition of d-cycloserine (DCS) versus pil placebo to a cognitive-behavioral program (CBT) targeting the role of anxiety sensitivity, distress intolerance, and panic attacks in smoking maintenance. The proposed project builds directly from our basic and clinical research as well as corresponding pilot work on (a) tobacco-panic relations; (b) intensive cognitive-behavioral intervention (CBT) for panic- and anxious-prone smokers; and (c) DCS enhancement of CBT for panic reduction. The project aims to obtain initial effect sizes and perform an initial test of putative mechanisms of our specialized behavioral group protocol, Panic and Smoking Reduction Treatment (PSRT), combined with DCS as compared to PSRT plus placebo. The PSRT program integrates interceptive exposure, cognitive restructuring, and psycho education exercises with standard smoking cessation strategies and nicotine replacement therapy. Adult smokers (n = 80) with panic attacks will be recruited and randomly assigned to either: (1) PSRT plus DCS or (2) PSRT plus pill placebo. Primary outcome measures will be point prevalence abstinence, time to first smoking lapse, and time to smoking relapse, assessed at 2, 4, 8, 10, 16, and 24 weeks after quit date. Proposed mediators include panic attacks, distress intolerance, anxiety sensitivity, nicotine withdrawal symptoms, and negative effect. These variables will be assessed at baseline, weekly during the treatment phase, and at 2, 4, 8, 10, 16, and 24 weeks after quit date. The proposed study represents a crucial and important stage in translating basic research to strategies for treating nicotine dependence. The investigation addresses an important public health issue by testing an integrated intervention --- informed by basic research --- that may lead to a more effective and efficient treatment for at-risk smokers while simultaneously isolating explanatory mechanisms. The expected findings should: (1) guide advances in the theoretical conceptualization of the mechanisms involved in panic- and anxiety-smoking relations; and (2) provide initial effect size data for the addition of DCS to an integrated psychosocial/behavioral and pharmacological smoking cessation intervention for smokers with panic attacks, and thus provide the necessary data for a large-scale follow-up trial.

**Title**: Dose timing of D-cycloserine to augment CBT for social anxiety disorder.
**PI**: Jasper Smits

**Dates**: 1-JUN-2014 to 31-MAY-2018
**Source**: National Institute of Mental Health
**Total costs**: $695,250
**Description**: This application is in response to PAR-12-071: Collaborative R34s for Pilot Studies of Innovative Treatments in Mental Disorders (Collaborative R34). D-cycloserine (DCS) is a partial N-methyl-D-aspartate glutamate agonist that has been shown to enhance exposure therapies for anxiety disorders. This approach is grounded in recent research advances in understanding the neural circuitry underlying fear extinction and is based upon one of the striking successes of translational research. All human clinical studies to date have administered DCS at least 1 hour prior to the exposure sessions. This dose-timing strategy limits the clinical utility of this highly promising augmentation strategy, especially sine accumulating research suggest that the efficacy of DCS for enhancing exposure therapy outcomes may depend on the success of exposure sessions. Pre-clinical and initial clinical data suggest that the DCS exposure-augmentation effect can also be obtained when DCS is administered immediately after an extinction trial when it follows successful exposure sessions. The proposed study builds upon this extant research by testing the efficacy of tailored post-session DCS administration (i.e., only following successful exposure sessions) for augmenting exposure therapy. In order to maintain high internal validity in this R34 study, we will enroll patients with social anxiety disorder (SAD) in a previously validated 5-session CBT protocol and randomize them to: (1) tailored post-session DCS administration; (2) pre-session DCS administration; (3) placebo administration; or (4) non-tailored post-session DCS administration. The primary outcomes will be short- and long-term improvements in social anxiety severity: We expect that the tailored post-session DCS administration condition will outperform the pre-session DCS administration, placebo administration, and non-tailored post-session DCS administration conditions, respectively, at posttreatment, 1-month and 3-month follow-up. In addition, we will explore potential moderators of the efficacy of tailored post-session DCS administration for augmenting exposure therapy. This application is the logical next step in the study of DCS. It provides an important innovative move toward the realization of personalized medicine by providing the first step in the eventual development of an algorithm for administering DCS in CBT with the goal of maximizing the efficacy and cost-effectiveness of therapy for anxiety disorders, which are some of the most prevalent mental conditions, making this a project of potentially high public health significance.

**Title**: Approach bias retraining to augment smoking cessation.
**PI**: Jasper Smits
**Dates**: Pending
**Source**: National Institute on Drug Abuse
**Total costs**: $$704,250
**Description**: Cigarette smoking remains a leading cause of preventable death, contributing to over 480,000 deaths each year. Although efficacious, standard care for smoking cessation is associated with high non-response rates, suggesting there is a need to develop augmentation strategies. Theory and empirical findings suggest that targeting automated, impulsive, implicit processes may hold promise. Specifically, retraining approach bias, or the approach action tendency toward stimuli related to the substance of interest has been effective in alcohol use disorders (i.e., reduction in relapse rates by 10%-13%). We recently extended this work to smoking by demonstrating that approach bias retraining reduced approach bias and the reduction in

approach bias was associated with the number of days quit in the week following a self-guided quit attempt. The goal of this application is to pilot test an intervention that integrates approach bias retraining with standard care for smoking cessation. The integrated intervention involves seven weekly 60-minute sessions. Each session involves 15 minutes of computerized approach bias retraining followed by 45 minutes of individual CBT. The target quit week is set at week 5, at which time nicotine replacement therapy is prescribed. Adult smokers (N=100) will be recruited and randomly assigned to (1) the integrated intervention or (2) a control intervention that combines standard smoking cessation care as described above with a computerized intervention that does not target approach bias. Abstinence will be assessed during the intervention (weeks 0- 7), at posttreatment (week 8), and at 1-month (week 9), 2-month (week 13) and 3-month (week 17) follow-up (i.e., post-quit). Measures of putative mediators will be assessed during the intervention (weeks 0-7).
The proposed study represents a crucial and important stage in translating basic research to strategies for treating nicotine dependence. The investigation addresses an important public health issue by testing an integrated intervention - informed by basic research - that may lead to a more effective treatment for at-risk smokers while simultaneously isolating explanatory mechanisms. The expected findings should: (1) guide advances in the theoretical conceptualization of the mechanisms involved smoking; and (2) provide initial effect size data for the integrated smoking cessation intervention, and thus provide the necessary data for a large- scale follow-up trial.

**Title**: Exercise as an aid to smoking cessation in anxiety vulnerable adults.
**PI**: Jasper Smits
**Dates**: 11/16/2016 to 11/15/2019
**Source**: Cancer Prevention Research Institute of Texas
**Total costs**: $891,623
**Description**: Cigarette smoking is the leading cause of death and disability in the United States. Although smoking has declined since 1964, it is still very common among some groups of people. One such group is persons with emotional symptoms and disorders. There has been little success in developing treatments for smoking cessation for smokers with affective disturbances. Recent work suggests that being sensitive to, and less tolerant of, stress is associated with many problems in daily life. People with high 'stress sensitivity' tend to use avoidant strategies to cope with their stress, like smoking. Also, people with high levels of stress sensitivity report stronger beliefs that smoking will reduce negative feelings. They also report having a harder time quitting and in fact, are less successful at doing so. This information suggests that stress sensitivity is important to target during smoking cessation treatment for smokers with affective vulnerabilities. This clinical trial will evaluate a treatment that integrates exercise to reduce stress sensitivity among high stress sensitive smokers. It builds directly from our recent work and we now seek to adapt it to a more accessible and sustainable application. Results will provide important information on the benefit of an integrated intervention that could be used in the community for smokers at great risk for relapse and who do not benefit from existing alternative treatments. This study is the first to test an intervention for stress sensitive smokers and has the potential to help at-risk individuals experience quitting success and, ultimately, reduce the burden of tobacco-related cancers in Texas.
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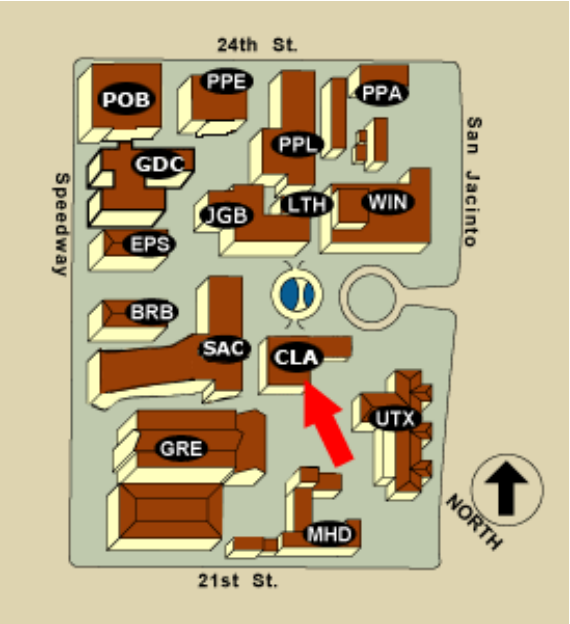
# Contact Information

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