BIOGRAPHICAL SKETCH

NAME: Leanne Williams, Ph.D.

eRA COMMONS USERNAME (credential, e.g., agency login): LEAWILLIAMS

POSITION TITLE: Vincent V.C. Woo Professor, Psychiatry and Behavioral Sciences, Stanford University

EDUCATION/TRAINING:

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Queensland, Australia	BA	03/1987	Psychology
University of New England, Australia	BA, First Class Honors	02/1990	Psychology
University of New England, with scholarship to Oxford University, UK	PhD	03/1996	Cognitive Neuroscience

A. Personal Statement

I am a clinical translational neuroscientist who has defined the emerging field of precision psychiatry by integrating brain-circuit-informed methods in diagnosis and treatment. Over the past 25 years, I have led innovations that bridge basic neuroscience and clinical care – establishing objective neural biomarkers to define diagnostic biotypes and predict personalized treatment outcomes, particularly for depression and anxiety. My leadership spans five key areas:

1. Establishing Normative Circuit-Based Assessments Across the Lifespan

I developed standardized neuroimaging and behavioral tasks grounded in cognitive and affective neuroscience, validated across ten decades of the human lifespan. These tools provide a transdiagnostic reference framework for quantifying brain function and are now applied across multiple large-scale clinical studies.

2. Uncovering the Neural Basis of Affective and Cognitive Dysfunction

Through multimodal integration of fMRI, EEG, physiology, and behavior, I have delineated circuit-level mechanisms that underlie affective and cognitive disturbances in depression and anxiety. In a recent NIMH U01 (2017–2022), I advanced this work by employing connectome-scale imaging in treatment-free individuals followed longitudinally. This work illuminated dynamic neural correlates of symptom trajectories.

3. Defining Neural Circuit Biotypes for Depression and Anxiety

Building on these findings, I proposed a taxonomy of brain-based biotypes – clinically relevant subgroups defined by distinct circuit dysfunctions – published in *The Lancet Psychiatry* (2016). I subsequently developed neuroimaging technology for quantifying circuit activity at the individual level, validated across discovery, independent replication, and treatment samples (*Biological Psychiatry*, 2022). This technology is currently covered by seven issued U.S. and international patents. It underpins our demonstration that biotypes are distinguished by specific clinical profiles and predict differential treatment outcomes (*Nature Medicine*, 2024), offering a biologically grounded alternative to diagnosis based on symptoms alone.

4. Personalized Treatment Translation Using Circuit-Based Biotypes

I have led multiple multi-site clinical trials using brain-based biotypes to predict personalized outcomes across a range of treatments, including antidepressants, behavioral therapies, repurposed medications, neuromodulation, and rapid-acting interventions. As academic PI of iSPOT-D, with 17 sites and more than 1,000 patients, I demonstrated that specific neural circuits predict differential response to antidepressants targeting serotonin, dopamine, and norepinephrine pathways. I built on this foundation in the ENGAGE UH2/UH3 trial (2016–2021), funded under NIH's Science of Behavior Change initiative, to identify behavioral therapy response predictors. I recently completed an R01 evaluating Transcranial Magnetic Stimulation (TMS) for a cognitive biotype of depression. Within a NIDA P50 Center of Excellence, I direct studies of rapid-acting agents, including ketamine, MDMA and psilocybin, for biotypes less responsive to traditional treatments. Most recently, I was awarded the U01 ACE-D trial under the NIMH IMPACT-MH initiative, which operationalizes biotype-driven precision psychiatry in real-world settings – further advancing the clinical translation of this framework.

5. Scientific Leadership and Mentorship

I have founded and led two major interdisciplinary centers: the Brain Dynamics Center at the University of Sydney (2002–2012) and the Stanford Center for Precision Mental Health and Wellness, launched in 2018. At Stanford, I also direct the Personalized and Translational Neuroscience Lab (PanLab) and the Precision Medicine Core at the VA Palo Alto MIRECC. In 2022, I was honored with the inaugural Vincent V.C. Woo Endowed Professorship. Mentorship remains central to my mission: I have trained 23 postdoctoral fellows at Stanford (including seven MD/PhDs), 11 postdoctoral fellows and 32 PhD students at Sydney, and 38 graduate students in total. Many now hold independent faculty positions and leadership positions, including women who have advanced to full professor and department chair. I have also served nationally as an external mentor through ACNP and the Career Development Institute for Psychiatry.

I highlight the following publications outlining circuit-based biotypes, implemented in my patented biotype image processing system that is now used by multiple labs and investigators:

1. **Williams LM** (2016). Precision Psychiatry: A neural circuit taxonomy for depression and anxiety. The Lancet Psychiatry, 3(5):472-480. PMID: 27150382 PMCID: PMC4922884. ESI Highly Cited Paper (Web of Science)
2. **Williams LM** (2017). Defining biotypes for depression and anxiety based on large-scale circuit dysfunction: a theoretical review of the evidence and future directions for clinical translation. Depress Anxiety, 34(1):9-24. PMID: 27653321 PMCID: PMC5702265. FWCI=8.73.

Ongoing and recently completed NIH funded projects I would like to highlight:

U01MH136062
05/2024–02/2029
Williams (contact MPI): ACE-D: Accelerating Cognition-guided signatures to Enhance translation in Depression

P50DA042012
08/2023–09/2028
Williams (Project PI): Neural circuit dynamics of drug action (Overall PI, Karl Deisseroth)

R01MH132962
09/2023–07/2028
Williams (MPI, with Sheline, University of Pennsylvania): Ascertaining Network Mechanisms and Analytics of Emotional Dysfunction (HARMONY)

R01MH120126
09/2019–05/2025
Williams (PI): Mechanistic circuit markers of transcranial magnetic stimulation outcomes in pharmacoresistant depression

U01MH109985
04/2017–04/2022
Williams (PI): Mapping connectomes for disordered emotional states

Indicators of impact and productivity

H-index	122
Number of peer-reviewed primary papers	403
Number of peer-reviewed papers as first author	59
Number of peer-reviewed papers as last (senior) author	169

B. Positions, Scientific Appointments, and Ho

Faculty and Scientific Leadership Positions

2018 – present	Founding Director of the Stanford Center for Precision Mental Health and Wellness
2018 – present	Associate Chair, Translational Neuroscience, Department of Psychiatry and Behavioral Neurosciences, Stanford University School of Medicine
2016 – 2018	Associate Chair, Research Strategy, Department of Psychiatry and Behavioral Neurosciences, Stanford University School of Medicine
2015 – 2018	Chair of Steering Committee for the Major Labs and Clinical Translational Neurosciences Incubator, Department of Psychiatry and Behavioral Neurosciences, Stanford
2013 – present	Professor, Psychiatry and Behavioral Sciences, Stanford University School of Medicine. Endowed as the Vincent V.C. Woo Professor of Psychiatry and Behavioral Sciences in 2022.
2013 – present	Founding Director, Stanford Personalized and Translational Neuroscience Lab (PanLab)
2012 – present	Director of Education and Precision Medicine Core, MIRECC VISN21, VA Palo Alto
2007 – 2013	Foundation Professor in Cognitive Neuropsychiatry, University of Sydney Medical School
2004 – 2006	Associate Professor, Psychiatry, University of Sydney Medical School
2002 – 2004	Associate Professor, Psychology, University of Sydney
2002 – 2012	Founding Director, Brain Dynamics Center, Sydney Medical School
1999 – 2001	Senior Lecturer (tenured position), Psychology, University of Sydney

Elected Professional Distinctions

2023 – 2026	Councillor-at-Large, Society of Biological Psychiatry (SOBP)
2013 – present	Fellow since 2018, American College of Neuropsychopharmacology (ACNP)
2013 – 2016	Executive member, ACNP membership committee

Board Positions

2025 – present	Scientific Advisory Board, Advanced Research and Invention Agency (ARIA), UK government Department for Science, Innovation and Technology
2025 – present	Scientific Advisory Board, Stanford Center for Clinical and Translational Research Award
2024 – present	Scientific Advisory Board, MD Anderson Neuroscience Program
2019 – 2022	Member, World Economic Forum Global Future Council on Technology for Mental Health
2016 – present	Advisory Board, Stanford Center for Neurobiological Imaging (CNI)
2015 – 2023	Member, Advisory Board, ONE MIND PsyberGuide, One Mind Institute
2009	Advisory Board, Pfizer Advisory Board for Ziprasidone

Honors

2025	The Perry Award (In memory of Samuel Wesley Perry III, MD), Weill Cornell Medicine
2023	Educator Award of the Society of Biological Psychiatry (SOBP)
2023	Chairman's Senior Faculty Mentor Award, Stanford School of Medicine
2022	George Thompson Award of the Society of Biological Psychiatry (SOBP) to the SOBP Women's Leadership Group
2022/23/24	Best Female Scientist Award, for research.com world ranking in top 1,000 of all female scientist across disciplines based on impact factor
2016	Chairman's Award for Advanced Contributions to Science, Stanford School of Medicine
2012	Ernst Strüngmann Award, "Schizophrenia evolution and synthesis"
2008	Presidential Award, US Society for Psychosomatic Medicine
2005	Pfizer Foundation Senior Research Fellowship ($1M, internationally competitive award for "high-risk/high reward" biomedical research; 1 or 2 awarded nationally per year)
2003	Australian Museum Eureka Prize for Science
2001	Young Investigator Award, International Schizophrenia Congress
2000	Senior Scientist Award, 10th Biennial Winter Workshop on Schizophrenia
1998	Wellcome-Ramaciotti Research Award for advanced study, London Institute of Psychiatry
1991	British Council Postgraduate Scholarship Award for PhD study at Oxford University, UK
1990	Australian Postgraduate Research Award, a federal scholarship awarded to Honors program graduates who are ranked nationally in the top 1% of applicants for graduate study
1989	Australian Psychological Society (APS) Prize for the most outstanding Honors year research dissertation. "Honors" is a 1-year post-bachelor's degree program comprising 60% independent research. The prize is awarded as equivalent to summa cum laude.

C. Contributions to Science

1. Discovering the mechanisms of healthy and pathological emotional brain function

In my fundamental research, I have developed and validated experimental paradigms to probe core human emotional and cognitive circuits. One key innovation was the creation of a new emotion processing task that captures both automatic processing and consciously evaluated responses, validated using signal detection metrics. I combined high-temporal resolution EEG, high-spatial resolution fMRI, and behavioral readouts, alongside concurrent physiological recordings, to establish objective, interpretable indicators of emotional responses that do not rely on self-report. These methods enabled new transdiagnostic insights into psychosis, ADHD, PTSD, and depression. I also demonstrated their relevance as modifiable targets in intervention studies. These paradigms are widely adopted across other research groups and diagnoses.

a. **Williams LM**, Liddell BJ, Rathjen J, Brown KJ, Gray J, Phillips M, Young A, Gordon E (2004). Mapping the time course of nonconscious and conscious perception of fear: an integration of central and peripheral measures. Human Brain Mapping, 21(2), 64-74. PMID: 14755594 PMCID: PMC6871876. FWCI=5.11.

b. Liddell BJ, Brown KJ, Kemp AH, Barton MJ, Das P, Peduto AS, Gordon E, **Williams LM** (2005). A direct brainstem-amygdala-cortical 'alarm' system for subliminal signals of fear. NeuroImage, 24(1):235-243. PMID: 15588615. FWCI=6.22.

c. **Williams LM**, Das P, Harris AW, Liddell BJ, Brammer MJ, Olivieri G, Skerrett D, Phillips ML, David AS, Peduto A, Gordon E (2004). Dysregulation of arousal and amygdala-prefrontal systems in paranoid schizophrenia. Am J Psychiatry, 161(3):480-489. PMID: 14992974. FWCI=6.02.

d. Symond MP, Harris AWF, Gordon E, **Williams LM** (2005). "Gamma synchrony" in first-episode schizophrenia: a disorder of temporal connectivity? American Journal of Psychiatry, 162(3), 459-465. PMID: 15741462. FWCI=6.02.2.

2. Integrative computational approaches to neural heterogeneity and trajectories in depression and related disorders

To better understand the neural heterogeneity of depression and related disorders, and to identify predictors of risk and prognosis, I have integrated multimodal neuroimaging data with behavioral, genetic, and clinical measures. Risk trajectories have been established across 10 decades of the human lifespan. Using causal modeling, I demonstrated how genetic variants interact with early life trauma to shape both the structure and function of neural circuits implicated in affective risk trajectories. Employing gradient boosted decision tree algorithms, I showed that individualized profiles of symptoms and neural features predict clinical outcomes in depression. By combining structural imaging with connectomics analysis, I identified core neuroanatomical features that map onto circuit-level dysfunction. These multi-modal brain-symptom models have contributed to the discovery of individualized, brain-based biomarkers for depression and related conditions.

a. **Williams LM**, Brown KJ, Palmer D, Liddell BJ, Kemp AH, Olivieri G, Peduto A, Gordon E (2006). The mellow years? neural basis of improving emotional stability over age. Journal of Neuroscience, 26(24):6422–6430. PMID: 16775129 PMCID: PMC6674038. FWCI=2.86
b. Gatt JM, Nemeroff CB, Dobson-Stone C, Paul RH, Bryant RA, Schofield PR, Gordon E, Kemp AH, **Williams LM** (2009). Interactions between BDNF Val66Met polymorphisms and early life stress predict brain and arousal pathways to syndromal depression and anxiety. Molecular Psychiatry, 14(7):681-695. PMID: 19153574. FWCI=12.19
c. Rajpurkar P, Yan J, Dass N, Vale V, Keller A, Irvin J, Taylor Z, Basu S, Ng A, **Williams LM** (2020). Evaluation of a machine learning model based on pretreatment symptoms and electroencephalographic features to predict outcomes of antidepressant treatment in adults with depression. JAMA Network Open, 3(6): e206653. PMID: 32568399 PMCID: PMC7309440. FWCI=2.87.
d. Korgaonkar MS, Fornito A, **Williams LM** (2014). Abnormal structural networks characterize Major Depressive Disorder: A connectome analysis. Biol Psychiatry, 76(7):567-574. PMID: 24690111 (focus of editorial). FWCI=6.83

3. Neural circuit-informed biomarker trials testing predictors of treatment outcomes in major depressive disorder

As academic principal investigator of the landmark iSPOT-D (International Study to Predict Optimized Treatment in Depression), I led efforts to identify and validate functional neuroimaging biomarkers that predict differential response to commonly prescribed antidepressants. These biomarkers have advanced the field by enabling individualized predictions, differentiating which patients are most likely to benefit from specific treatments. The trial also established innovative, scalable methods for integrating neuroimaging into biomarker-guided designs, including the use of harmonized imaging protocols and NIH Common Data Elements targeting emotion- and cognition-related neural circuits.

a. **Williams LM**, Korgaonkar MS, Song YC, Paton R, Eagles S, Etkin A, Gordon E (2015). Amygdala reactivity to emotional faces in the prediction of general and medication-specific responses to antidepressant treatment in the randomized iSPOT-D trial. Neuropsychopharmacology, 40(10):2398-2408. PMID: 25824424 PMCID: PMC4538354. FWCI=5.81
b. Goldstein-Piekarski AN, Korgaonkar MS, Green E, Suppes T, Schatzberg AF, Hastie T, Nemeroff CB, **Williams LM** (2016). Human amygdala engagement moderated by early life stress exposure is a biobehavioral target for predicting recovery on antidepressants. Proceedings of the National Academy of Sciences, 113(42):11955-11960. PMID: 27791054 PMCID: PMC5081583. FWCI=1.49
c. Korgaonkar MS, Goldstein-Piekarski AN, Fornito A, **Williams LM** (2019). Intrinsic connectomes are a predictive biomarker of remission in major depressive disorder. Molecular Psychiatry, 25(7):1537-1549. PMID: 31695168 PMCID: PMC7303006. FWCI=5.42
d. Tozzi L, Goldstein-Piekarski AN, Korgaonkar MS, **Williams LM** (2020). Connectivity of the cognitive control network during response inhibition as a predictive and response biomarker in major depression: Evidence from a randomized clinical trial. Biological Psychiatry, 87(5):462-472. PMCID: PMC8628639. FWCI=5.42.

4. Pioneering brain-based biotypes

I have led the development of experimental and computational approaches to parse the heterogeneity of depression into brain-based biotypes—clinically meaningful subgroups defined by distinct patterns of circuit dysfunction. In this personalized approach, the individual– not the diagnostic label – is the primary statistical unit. I pioneered a method for quantifying functional neuroimaging data at the individual level using normative modeling, analogous to neuropsychological testing, to position each person relative to a reference distribution derived from healthy controls. This yields intuitive personalized brain circuit scores. Applying this framework, we identified and validated six reproducible biotypes of depression and anxiety. These biotypes differ in specific symptoms, behavior and treatment response profiles.

They are stable at the individual level, providing actionable targets for intervention and a foundation for stratified precision medicine trial designs.

a. Grisanzio KA, Goldstein-Piekarski AN, Wang MY, Ahmed APR, Samara Z, **Williams LM** (2018). Transdiagnostic symptom clusters and associations with brain, behavior, and daily function across mood, anxiety, and trauma disorders. JAMA Psychiatry, 75(2):201-209. PMID: 29197929 PMCID: PMC5838569. FWCI=6.64.
b. Goldstein-Piekarski AN, Ball TM, Samara Z, Staveland BR, Keller AS, Fleming SL, Grisanzio KA, Holt-Gosselin B, Stetz P, Ma J, **Williams LM** (2022). Mapping neural circuit biotypes to symptoms and behavioral dimensions of depression and anxiety. Biol Psychiatry, 91(6):561-571. PMCID: PMC9511971. FWCI=6.99.
c. Hack LM, Tozzi L, Zenteno S, Olmsted AM, Hilton, Jubeir J, Korgaonkar MS, Schatzberg AF, Yesavage JA, O'Hara R, **Williams LM** (2023). A cognitive biotype of depression linking symptoms, behavior measures, neural circuits, and differential treatment outcomes: A randomized clinical trial. JAMA Network Open, 6(6): e2318411. PMID: 37318808 PMCID: PMC10273022. FWCI=12.09
d. Tozzi L, Zhang X, Pines A, Olmsted AM, Zhai ES, Anene ET, Chesnut M, Holt-Gosselin B, Chang S, Stetz PC, Ramirez CA, Hack LM, Korgaonkar MS, Wintermark M, Gotlib IH, Ma J, **Williams LM** (2024). Personalized brain circuit scores identify clinically distinct biotypes in depression and anxiety. Nature Medicine, 30(7):2076-2087. PMID: 38886626 PMCID: PMC11271415, ESI Highly Cited Paper (Web of Science). FWCI=16.48.

5. Advancing precision psychiatry: Using biotypes to guide personalized treatment in depression

I have developed and applied circuit-based biotypes to enable more precise, personalized treatment selection for individuals with depression. This approach supports prospective stratification of patients into biotypes based on individual neural circuit profiles, each targeted with specific treatments. Guided by this framework, treatments have spanned standard antidepressants, repurposed medications, rapid-acting agents, and neuromodulation. Across multiple studies, we have shown that circuit biotypes serve as differential predictors of treatment success: matching patients to treatments based on their circuit profiles can double response and remission rates. This approach also identifies individuals unlikely to benefit from standard antidepressants and predicts which alternative treatments they are most likely to respond to. For example, we characterized a cognitive biotype of depression marked by hypoactivity in the cognitive control circuit—associated with poor response to antidepressants but favorable outcomes with transcranial magnetic stimulation (TMS). This work is now being implemented in clinical care through the Precision Mental Health Clinic I co-founded with clinical faculty colleagues.

a. Hack L, Jubeir J, Hilton R, Tozzi L, Boyar L, Zhang X, Lyons T, Jo B, O'Hara R, Schatzberg A, **Williams LM** (accepted June 29, 2025). Stratified Precision Medicine Trial Targeting Selective Mechanisms of Alpha 2A Agonism as a Treatment for the Cognitive Biotype of Depression: The BIomarker Guided (BIG) Study for Depression. Research Square [Preprint]. 2025 Feb 27:rs.3.rs-5762756. PMID: 40060043; PMCID: PMC11888545.
b. Tozzi L, Bertrand C, Hack LM, Lyons T, Olmsted AM, Rajasekharan D, Chen T, Berlow YA, Yesavage JA, Lim K, Madore M, Philip NS, Holtzheimer P, **Williams LM** (2024). A cognitive neural circuit biotype of depression showing functional and behavioral improvement after transcranial magnetic stimulation in the B-SMART-fMRI trial. Nature Mental Health, 2:987-998. PMID: 39911692 PMCID: PMC11798407. FWCI=1.38
c. Zhang X, Pines A, Stetz P, Goldstein-Piekarski AN, Xiao L, Lv N, Tozzi L, Lavori PW, Snowden MD, Venditti EM, Smyth JM, Suppes T, Ajilore O, Ma J, **Williams LM** (2024). Adaptive cognitive control circuit changes associated with the problem-solving ability and depression symptom outcomes over 24 months. Science Translational Medicine, 16(763):eadh3172. PMID: 3923124. FWCI=1.41
d. Zhang X, Hack LM, Bertrand C, Hilton R, Gray NJ, Boyar L, Laudie J, Heifets BD, Suppes T, van Roessel PJ, Rodriguez CI, Deisseroth K, Knutson B, **Williams LM** (2025). Negative Affect Circuit Subtypes and Neural, Behavioral, and Affective Responses to MDMA: A Randomized Clinical Trial. JAMA Network Open, 8(4):e257803. PMID: 40305021; PMCID: PMC12044494.

FWCI= Scopus Field-Weighted Citation Impact (FWCI), a normalized metric indicating how citations of a publication compare to the global average for similar publications. A score >1.0 reflects above-average impact.

Complete list of published work. For the list of over 400 publications included in MyBibliography on NCBI: https://www.ncbi.nlm.nih.gov/myncbi/1BaGkg3Fizwkx/bibliography/public/