BIOGRAPHICAL SKETCH

Provide the following information for the PI, Senior/key personnel and other significant contributors.
DO NOT EXCEED FOUR PAGES.

NAME	POSITION TITLE
Michael E. Cahill	Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Lawrence University (Appleton, WI)	B.A.	09/1997-06/2001	Neuroscience & Psychology
Northwestern University (Evanston & Chicago, IL)	Ph.D.	09/2005-09/2011	Neuroscience
Icahn School of Medicine at Mount Sinai, (NY, NY)	Postdoc.	09/2011-02/2017	Neurobiology
University of Wisconsin at Madison (Madison, WI)	Assistant Professor	04/2017-Present	Neuroscience

A. Personal Statement

Over the past 12 years, my research has focused on delineating the molecular and biochemical mechanisms that regulate dendritic spine plasticity, and in particular, understanding how alterations in synaptic plasticity contribute to specific behavioral phenotypes relevant to the study of neuropsychiatric disorders. During my career, I have identified novel functions, modes of regulation, and interacting partners of disease-associated proteins in dendritic spines, and as dendritic spine aberrations are a prominent feature of numerous neuropsychiatric disorders, including autism, this continued effort remains an important area of research. My research approach over the past decade has been to determine how genetic findings implicated in neuropsychiatric disorders impact associated protein function, and how altered protein function, in turn, impacts neuronal ultrastructure, neuronal function, and behavioral phenotypes. During my graduate work in the laboratory of Peter Penzes, I modeled the impact of a gene implicated in schizophrenia by creating the first genetically-modified mouse of this gene, and determined the consequent effects on synaptic structure and function, and on specific disease-associated behavioral endophenotypes. I then lead efforts that identified novel synaptic complexes and signal transduction pathways that the associated protein product of this gene functions in, and characterized the functional outcome of a rare coding mutation in this gene we subsequently identified in a schizophrenia subject.

My postdoctoral work in Eric Nestler's laboratory focused on understanding the synaptic contribution to addiction behavioral phenotypes. Rather than modeling human genetic alterations associated with an increased propensity to addiction, I modeled aspects of human drug consumption behavior in rodents, and then worked backwards to determine the underlying genomic alterations that drive addiction synaptic and behavioral phenotypes. I accomplished this by employing next-generation genome-wide RNA-sequencing to assess the transcription profile of brain reward regions following cocaine intake as an unbiased way to identify genes and associated protein products involved in reward signaling. Using this approach, I identified and characterized a signal transduction pathway that defines the mechanisms by which nuclear to synaptic interactions influence dendritic spine plasticity, and determined how this altered synaptic plasticity in brain reward regions, in turn, drives addiction-relevant behavior. Moreover, I used *in vivo* optogenetics to understand how the dynamic regulation of functional connectivity are related to specific behavioral endpoints.

The focus of my laboratory will be to understanding how alterations in dendritic spine formation, stability, and plasticity contribute to the etiology of schizophrenia, autism, and depression. Particular attention will be devoted to understanding how alterations in the functional connectivity between brain regions give rise to the synaptic structural hallmarks and behavioral phenotypes of these disorders. Further, my laboratory seeks to identify final common signal transduction pathways that multiple genes identified in these disorders function in. Finally, my work will seek to understand the biological underpinnings of sex differences in disease etiology and pathogenesis, and to understand how prenatal maternal factors affect disease transmission to her progeny. These approaches could help illuminate potential future therapeutic molecular targets.

B. Positions and Honors

Scientific employment:

2000	Research Internship, University of Illinois at Chicago, Department of Anatomy and Cell Biology, Chicago, IL
2001-2003	Research Technologist, Northwestern University Department of Medicine, Division of Hepatology, Chicago, IL
2003-2005	Research Technologist, Northwestern University Feinberg School of Medicine, Department of Cell and Molecular Biology, Chicago, IL
2005-2011	Doctoral Student, Northwestern University Interdepartmental Neuroscience program, Chicago and Evanston, IL
2011-	Postdoctoral Fellow, Icahn School of Medicine at Mount Sinai, New York, NY

Honors:

2000	Elected into Psi Chi International Honor Society
2001	Bachelor of Arts *cum laude*
2006-2008	Neuroscience in the early years grant recipient (National Institute of Health)
2009-2011	Ruth L. Kirschstein National Research Service Awards (NRSA) for Individual Predoctoral Fellows
2015	Selected to give a press conference presentation at the Society for Neuroscience Annual Meeting
2015	Invited featured speaker at the American Academy for the Advancement of Science (AAAS) annual meeting
2016	NARSAD Young Investigator Award

C. Contributions to Science

A URL to a full list of my published work is listed below.

https://www.ncbi.nlm.nih.gov/sites/myncbi/18ollWdWTMWk5/bibliography/53230290/public/?sort=date&direction=descending

D. Research Support

Ongoing Research Support

NARSAD Young Investigator Award ($35,000 yearly) Michael Cahill (PI) 01/15/2017-01/14/2019
This proposal aims to determine how local synaptic translation signaling impacts synaptic connectivity *in vivo* and executive processing.

Completed Research Support

NIH 1F31AG031621-01A2 ($28,000 yearly) Michael Cahill (PI) 04/1/09-03/31/11
Ruth L. Kirschstein National Research Service Awards (NRSA) for Individual Predoctoral Fellows.
The goal of this project was to determine the role for the RacGEF kalirin in regulating dendritic spine morphogenesis, synaptic function, and disease-related behavioral phenotypes *in vivo*. 85% of time per 12-month calendar year dedicated.

NIH 5T32AG020418-09 ($25,000 yearly) Michael Cahill (PI) 09/1/06-09/1/08
NIH Neuroscience in the Early Years: Predoctoral Training at Northwestern University
This award is given based on scientific research promise exhibited during the first year of the neuroscience Ph.D. program, with the goal to foster collaborations between the student and multiple research faculty. 85% of time per 12- month calendar year dedicated.

E. Full list of peer-reviewed papers (in order of publication year)

1. **Cahill ME**, Walker DM, Gancarz AM, Wang ZJ, Lardner CK, Bagot RC, Neve RL, Dietz DM, Nestler EJ. The dendritic spine morphogenic effects of repeated cocaine use occur through the regulation of serum response factor (SRF) signaling. *Molecular Psychiatry* (2017) (in press)

2. Labonté B, Engmann O, Purushothaman I, Menard C, Wang J, Tan C, Scarpa JR, Moy G, Loh YE, **Cahill M**, Lorsch ZS, Hamilton PJ, Calipari ES, Hodes GE, Issler O, Kronman H, Pfau M, Obradovic ALJ, Dong Y, Neve RL, Russo S, Kazarskis A, Tamminga C, Mechawar N, Turecki G, Zhang B, Shen L, Nestler EJ. Sex-specific transcriptional signatures in human depression. *Nature Medicine* (2017) 23(9) 1102-1111.

3. Ceglia I, Lee KW*, **Cahill ME***, Graves SM, Dietz D, Surmeier DJ, Nestler EJ, Nairn AC, Greengard P, Kim Y. WAVE1 in neurons expressing the D1 dopamine receptor regulates cellular and behavioral actions of cocaine. *Proceedings of the National Academy of the Sciences* (2017) 114 (6): 1395-1400.
*Co-first authorship

4. Calipari ES, Juarez B, Morel C, Walker DM, **Cahill ME**, Ribeiro E, Roman-Ortiz C, Ramakrishnan C, Deisseroth K, Han MH, Nestler EJ. Dopaminergic dynamics underlying sex-specific cocaine reward. *Nature Communications* (2017) 8: 13877.

5. Damez-Werno D, Sun H, Socobe KN, Shao N, Rabkin J, Dias C, Calipari ES, Maze I, Pena CJ, Walker DM, **Cahill ME**, Chandra R, Gancarz A, Mouzon E, Landry JA, Cates H, Lobo MK, Dietz D, Allis CD, Guccione E, Turecki G, Defilippi P, Neve RL, Hurd YL, Shen L, Nestler EJ. Histone arginine methylation in cocaine action in the nucleus accumbens. *Proceedings of the National Academy of the Sciences* (2016) 113 (34): 9623-9628.

6. **Cahill ME**, Bagot RC, Gancarz AM, Walker DM, Sun H, Wang Z, Heller EA, Feng J, Kennedy PJ, Koo JW, Cates HM, Neve RL, Shen L, Dietz DM, Nestler EJ. Bidirectional synaptic structural plasticity after chronic cocaine administration occurs through Rap1 small GTPase signaling. *Neuron* (2016) 89: 566-582.

7. Heshmati M, Golden SA, Pfau ML, Christoffel DJ, Seeley EL, **Cahill ME**, Khibnik LA, Russo SJ. Mefloquine in the nucleus accumbens promotes social avoidance and anxiety-like behavior in mice. *Neuropharmacology* (2015) 101: 351-357.

8. Sun H, Damez-Werno DM, Scobie KN, Shao N, Dias C, Rabkin J, Koo JW, Korb E, Bagot RC, Ahn FH, **Cahill ME**, Labonté B, Mouzon E, Heller EA, Cate H, Golden SA, Gleason K, Russo SJ, Andrews S, Neve R, Kennedy PJ, Maze I, Dietz DM, Allis CD, Turecki G, Varga-Weisz P, Tamminga C, Shen L, Nestler EJ. ACF chromatin-remodeling complex mediates stress-induced depressive-like behavior. *Nature Medicine* (2015) 21: 1146-1153.

9. Feng J, Shao N, Szulwach K, Vialou V, Huynh J, Zhone C, Le T, Ferguson D, **Cahill ME**, Li Y, Koo JW, Ribeiro E, Labonte B, Laitman B, Estey D, Stockman V, Kennedy P, Courousse T, Mensah I, Turecki G, Faull K, Song H, Fan G, Casaccia P, Shen L, Jin P, Nestler EJ. Role of Tet1 and 5-hydroxymethylcytosine in cocaine action. *Nature Neuroscience* (2015) 18: 536-544.

10. Koo JW, Mazei-Robison M, LaPlant Q, Egervari G, Braunscheidel K, Adank D, Ferguson D, Feng J, Sun H, Scobie K, Damez-Werno D. Riberio E, Pena C, Walker D, Bagot R, **Cahill ME**, Anderson SA, Labonte B, Hodes G, Browne H, Chadwick B, Robison A, Vialou V, Dias C, Lorsch Z, Mouzon E, Lobo MK, Dietz D, Russo S, Neve R., Hurd Y, Nestler EJ. Epigenetic basis of opiate suppression of Bdnf gene expression in the ventral tegmental area. *Nature Neuroscience* (2015) 18: 415-422.

11. Russell TA, Blizinsky KD, Cobia DJ**, Cahill ME**, Xie Z, Sweet RA, Duan J, Gejman PV, Wang L, Csernansky JG, Penzes P. A sequence variant in human KALRN impairs protein function and coincides with reduced cortical thickness. *Nature Communications* (2014) 5: 4858

12. Feng J, Wilkinson M, Liu X, Purushothaman I, Ferguson D, Vialou V, Maze I, Shao N, Kennedy P, Koo J, Dias C, Laitman B, Stockman V, Laplant Q, **Cahill ME**, Nestler EJ, Shen L. Chronic cocaine-regulated epigenomic changes in mouse nucleus accumbens. *Genome Biology* (2014) 15: R65

13. Vialou V, Bagot RC, **Cahill ME**, Ferguson D, Robison AJ, Dietz DM, Fallon B, Mazei-Robison M, Ku SM, Harrigan E, Winstanley CA, Joshi T, Feng J, Berton O, Nestler EJ. Prefrontal Cortical Circuit for Depression- and Anxiety-Related Behaviors Mediated by Cholecystokinin: Role of ΔFosB. *Journal of Neuroscience* (2014) 34: 3878-3887.

14. Wang X, **Cahill ME**, Werner CT, Christoffel DJ, Golden SA, Xie Z, Loweth JA, Marinelli M, Russo SJ, Penzes P, Wolf ME. Kalirin-7 mediates cocaine-induced AMPA receptor and spine plasticity, enabling incentive sensitization. *Journal of Neuroscience* (2013) 33: 11012-11022.

15. **Cahill ME**, Reemers C, Jones KA, Xie Z, Sweet RA, Penzes P. Neuregulin1 signaling promotes dendritic spine growth through kalirin. *Journal of Neurochemistry* (2013) 126: 625-635.

16. Golden SA, Christoffel DJ, Heshmati M, Hodes GE, Magida J, Davis K, **Cahill ME**, Dias C, Ribeiro E, Ables JL, Kennedy PJ, Robison AJ, Gonzalez-Maeso J, Neve RL, Turecki G, Ghose S, Tamminga CA, Russo SJ. Epigenetic regulation of RAC1 induces synaptic remodeling in stress disorders and depression. *Nature Medicine* (2013) 19: 337-344.

17. Srivastava DP, Copits BA, Xie Z, Huda R, Jones KA, Mukherji S, **Cahill ME**, Vanleeuwen JE, Woolfrey KM, Rafalovich I, Swanson GT, Penzes P. Afadin is required for maintenance of dendritic structure and excitatory tone. *Journal of Biological Chemistry* (2012) 287: 35964-35974.

18. Dietz DM, Sun H, Lobo MK, **Cahill ME**, Chadwick B, Gao V, Koo JW, Mazei-Robison MS, Dias C, Maze I, Damez-Werno D, Dietz KC, Scobie KN, Ferguson D, Christoffel D, Ohnishi Y, Hodes GE, Zheng Y, Neve RL, Hahn KM, Russo SJ, Nestler EJ. Rac1 is essential in cocaine-induced structural plasticity of nucleus accumbens neurons. *Nature Neuroscience* (2012) 15: 891-896.

19. Nicholson DA, **Cahill ME***, Tulisiak CT, Geinisman Y, Penzes P. Spatially restricted actin-regulatory signaling contributes to synapse morphology. *Journal of Neurochemistry* (2012) 121: 852-860.
*Co-first authorship

20. Penzes P, **Cahill ME**. Deconstructing the signal transduction pathways the regulate the actin cytoskeleton in dendritic spines. *Cytoskeleton* (2012) 69: 426-441.

21. Deo AJ, **Cahill ME**, Li S, Goldszer I, Henteleff R., VanLeeuwen JE, Rafalovich I, Gao R, Stachowski EK, Sampson AR, Lewis DA, Penzes P, Sweet RA. Increased expression of kalirin-9 in the auditory cortex of schizophrenia subjects: its role in dendritic pathology. *Neurobiology of Disease* (2012) 45: 796-803.

22. **Cahill ME**, Jones KA, Rafalovich I, Xie Z, Barros CS, Müller U, Penzes P. Control of interneuron dendritic growth through NRG1/erbB4-mediated kalirin-7 disinhibition. *Molecular Psychiatry* (2012) 17: 99-107.

23. Penzes P, **Cahill ME**, Jones KA, VanLeeuwen JE, Woolfrey KM. Dendritic spine pathology in neuropsychiatric disorders. *Nature Neuroscience* (2011) 14: 285-293.

24. Xie Z, **Cahill ME***, Radulovic J, Wang J, Campbell SL, Miller CA, Sweatt JD, Penzes P. Hippocampal phenotypes in kalirin-deficient mice. *Molecular and Cellular Neuroscience* (2011) 46: 45-54.
*Co-first authorship

25. **Cahill ME**, Xie Z, Day M, Barbolina MV, Photowala H, Miller CA, Weiss C, Radulovic J, Sweatt JD, Disterhoft JF, Surmeier DJ, Penzes P. Kalirin regulates cortical spine morphogenesis and disease-related behavioral phenotypes. *Proceedings of the National Academy of the Sciences* (2009) 106: 13058-13063.

26. Xie Z, **Cahill ME**, Penzes P. Kalirin loss results in cortical morphological alterations. *Molecular and Cellular Neuroscience* (2009) 43: 81-89.

27. Woolfey KM, Srivastava DP, Photowala H, Yamashita M, Barbolina MV, **Cahill ME**, Xie Z, Jones KA, Quilliam LA, Prakriya M, Penzes P. Epac2 induces synapse remodeling and depression and its disease-associated forms alter spines. *Nature Neuroscience* (2009) 12: 1275-1284.

28. Penzes P, **Cahill ME**, Jones KA, Srivastava DP. Convergent CaMK and RacGEF signals control dendritic structure and function. *Trends in Cell Biology* (2008) 18: 405-413

29. Xie Z, Photowala H, **Cahill ME**, Srivastava DP, Woolfrey KM, Shum CY, Huganir RL, Penzes P. Coordination of synaptic adhesion with dendritic spine remodeling by AF-6 and kalirin-7. *Journal of Neuroscience* (2008) 28: 6079-6091.

30. Xie Z, Srivastava DP, Photowala H, Kai L, **Cahill ME**, Woolfrey KM, Shum CY, Surmeier DJ, Penzes P. Kalirin-7 controls activity-dependent structural and functional plasticity of dendritic spines. *Neuron* (2007) 56: 640-656.

31. Guillozet-Bongaarts AL, Glajch KE, Libson EG, **Cahill ME**, Bigio E, Berry RW, Binder LI. Phosphorylation and cleavage of tau in non-AD tauopathies. *Acta Neuropathologica* (2007) 113: 513-520.

32. Guillozet-Bongaarts AL, **Cahill ME**, Cryns VL, Reynolds MR, Berry RW, Binder LI. Pseudophosphorylation of tau at serine 422 inhibits caspase cleavage: in vitro evidence and implications for tangle formation in vivo. *Journal of Neurochemistry (2006)* 97: 1005-1014.

33. Guillozet-Bongaarts AL, Garcia-Sierra F, Reynolds MR, Horowitz PM, Fu Y, Wang T, **Cahill ME**, Bigio EH, Berry RW, Binder LI. Tau truncation during neurofibrillary tangle evolution in Alzheimer's disease. *Neurobiology of Aging (2005)* 26: 1015-1022.

34. Vaquero J, Chung C, **Cahill ME**, Blei AT. Pathogenesis of hepatic encephalopathy in acute liver failure. *Seminars in Liver Disease* (2003) 23: 259-269.

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