

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: **Michael Lloyd Perlis**

eRA COMMONS USER NAME: **mperlis**

POSITION TITLE: **Associate Professor, Psychiatry (Primary), School of Nursing (Secondary)**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Guilford College, Greensboro, North Carolina	B.A.	06/1983	Religious Studies
University of Arizona, Department of Psychology. Tucson, Arizona Mentor: Richard Bootzin, PhD	M.A.	06/1990	Psychology
Brown University, Alpert Medical School Clinical Mentor: Donn Posner PhD		06/1994	Clinical Internship
University of Arizona, Department of Psychology. Tucson, Arizona Mentor: Richard Bootzin, PhD	Ph.D.	06/1994	Clinical Psychology
Western Psychiatric Institute and Clinics University of Pittsburgh Mentors: Daniel Buysse MD & Michael Thase MD		07/1996	Research Post-Doctoral Fellowship

A. Personal Statement

My research program pertains to Insomnia and Behavioral Sleep Medicine. My specific research interests include: behavior, cognitive, and physiologic factors in acute and chronic insomnia, cortical arousal and conditioned CNS activation as a primary perpetuator of chronic insomnia; sensory and information processing and long term memory formation as key features of Insomnia Disorder; insomnia as a hybrid state between wake and sleep; sleep homeostasis effects on the frequency and severity of insomnia (and the patterning of insomnia over time); the relative efficacy of behavioral and pharmacologic treatments of insomnia; insomnia as risk factor for new onset and recurrent depression; the anti-depressant effects of CBT-I; and the potential of conditioning and partial reinforcement with placebos (behavioral pharmacotherapeutics) as a means to change how medical maintenance therapy is conducted for insomnia and other chronic conditions.

I have served as a PI or Co-PI on eight NIH funded studies (4 R01s and 3 R21s and 1 R03) and have mentored or co-mentored 7 additional NIH projects.

B. Positions and Honors

1985-1987	Research Assistant/Laboratory Technician to Wallace Mendelson, MD Section on Sleep Studies, National Institute of Mental Health, Bethesda, MD
1987-1988	Research Assistant/Laboratory Technician to Steven James, MD Sleep-Wake Disorders and Human Chronobiology, University of Pennsylvania, Philadelphia, PA
1988-1993	Research Associate/Laboratory Coordinator to Richard Bootzin, PhD Sleep Research Laboratory, Department of Psychology, University of Arizona, Tucson, AZ
1993-1994	Research Associate to Mary Carskadon, PhD Sleep Research Laboratory, E.P. Bradley Hospital, Brown University, Providence, RI
1996-2003	Assistant Professor, Department of Psychiatry, University of Rochester, Rochester, NY
1996-2001	Assistant Director, University of Rochester Sleep Research Laboratory, Rochester, NY
1996-1998	Co-Director, Behavioral Sleep Medicine Clinic, Sleep Disorders Center of Rochester
2001-2008	Director, University of Rochester Sleep Research Laboratory, Rochester, NY
2003-2008	Member, UR Neurosciences Program, Rochester, NY
2006-2012	Visiting Professor, Section of Psychological Medicine, Glasgow University, Glasgow Scotland

2006-2012 Visiting Professor, Department of Psychiatry, University of Freiburg, Freiburg Germany
 2008-2012 Visiting Professor, Department of Psychology, Northumbria University, New Castle England
 2008- Associate Professor, Department of Psychiatry, University of Pennsylvania, Philadelphia, PA
 2008- Director, University of Pennsylvania Behavioral Sleep Medicine Program, Philadelphia, PA
 2010- Secondary Appointment, School of Nursing, University of Pennsylvania, Philadelphia, PA

HONORS

1986 Award for Work Excellence, National Institute of Mental Health
 1989-1996 Sleep Research Society Conference Travel Awards,
 1990-1993 Academic Scholarships - Tuition Waivers, University of Arizona
 1991 & 1995 Sleep Research Society International Conference Travel Awards
 1995 Nomination: American Sleep Disorders Association's
 Young Investigator Award
 1996 Nomination: American Sleep Disorders Association's
 Young Investigator Award
 2000 Certificate of Meritorious Service as the Assistant
 Director of Training: Sleep Research Society
 2002-2005 NIH Clinical Research Scientist LRP Award
 2010 Recognition Award for the collaborative establishment of the
 Society of Behavioral Sleep Medicine (SBSM).
 2011 Recognition Award for service as the first president for the
 Society of Behavioral Sleep Medicine (SBSM).

C. Contribution to Science

My primary research agenda has been primarily on the topic of sleep continuity disturbance and insomnia. While narrow in focus, I have attempted to have a wide depth of field that embraces basic research, human experimental research, clinical research, and epidemiology. My efforts as a principle investigator, represented by over 111 peer reviewed publications, have been primarily in the human experimental and clinical research domains. My collaborations have allowed me to expand my program of research to include the polar ends of the spectrum (basic research and epidemiology). This work, while nascent, includes collaborations on drosophila and rodent models of acute and chronic insomnia and epidemiologic studies on the natural history of insomnia (from good sleep to chronic insomnia) and the effort to discriminate between the phenomenon of short sleep and the clinical problem of insomnia. My specific contributions are as follows.

1. **Developed the Neurocognitive Model of Insomnia (NMI) and contributed to the widespread dissemination of theoretical perspectives on insomnia as a disorder.** The NMI was the first model to conceptualize insomnia as a disorder using a cognitive neuroscience perspective, i.e., framing the disorder in terms of abnormal sensory and information processing and the attenuation of the normal mesograde amnesia of sleep. Viewed this way, insomnia may be characterized as hybrid state (part wake and part sleep) and in so doing gives rise to novel perspectives on etiology, pathophysiology, and treatment efficacy. Efforts within this arena contributed to my invitation to review the state of the science with respect to insomnia models for the last three Principles and Practice of Sleep Medicine texts. This effort has allowed for the concepts within the models to become "mainstreamed".
 - a) Perlis ML, Giles DE, Mendelson WB, Bootzin RR, Wyatt JK. Psychophysiological insomnia: the behavioral model and a neurocognitive perspective. *J Sleep Res.* 1997 Sep;6(3):179-88. Review. PMID: 9358396.
 - b) Perlis ML, Smith MT, Orff HJ, Andrews PJ, Giles DE. The mesograde amnesia of sleep may be attenuated in subjects with primary insomnia. *Physiol Behav.* 2001 Sep 1-15;74(1-2):71-6. PMID: 11564454.
2. **Contributed to the literature regarding the assessment of cortical arousal during sleep in terms of alpha, beta, and gamma EEG activity.** This work began by evaluating the potential association of "alpha sleep" to sensory and information processing and long term memory for episodic events during NREM. This investigation set the stage for the neurocognitive model and led to several investigations about beta and gamma activity in patients with insomnia. Four articles are provided below.
 - a. Parsons LC, Crosby LJ, Perlis M, Britt T, Jones P. Longitudinal sleep EEG power spectral analysis studies in adolescents with minor head injury. *J Neurotrauma.* 1997 Aug;14(8):549-59. PubMed PMID: 9300565.

- b. Perlis ML, Giles DE, Bootzin RR, Dikman ZV, Fleming GM, Drummond SP, Rose MW. Alpha sleep and information processing, perception of sleep, pain, and arousability in fibromyalgia. *Int J Neurosci*. 1997 Feb;89(3-4):265-80. PubMed PMID: 9134461.
 - c. Perlis ML, Kehr EL, Smith MT, Andrews PJ, Orff H, Giles DE. Temporal and stagewise distribution of high frequency EEG activity in patients with primary and secondary insomnia and in good sleeper controls. *J Sleep Res*. 2001 Jun;10(2):93-104. PubMed PMID: 11422723.
 - d. Perlis ML, Smith MT, Andrews PJ, Orff H, Giles DE. Beta/Gamma EEG activity in patients with primary and secondary insomnia and good sleeper controls. *Sleep*. 2001 Feb 1;24(1):110-7. PubMed PMID: 11204046.
3. **Contributed to the evaluation and standardization of CBT-I, the dissemination and implementation of this treatment modality, and the establishment of Behavioral Sleep Medicine as a sub-discipline of Sleep Medicine and Health Psychology.** This was primarily accomplished by publishing two of the first text books in Behavioral Sleep Medicine (ISBN-10: 0123815223 & ISBN-10: 0471443433) and the publication of a session by session treatment manual (ISBN-10:0387774408). Additionally, five articles served to push forward this agenda. One article was a comparative meta-analysis evaluating the relative efficacy of CBT-I as compared to medical interventions; two articles which demonstrated that in-clinic effects were equal to, or better than, the meta-analytic norms (one of which is cited below); and two articles which served to highlight issues around the history and future of Behavioral Sleep Medicine.
- a. Smith MT, Perlis ML, Park A, Smith MS, Pennington J, Giles DE, Buysse DJ. Comparative meta-analysis of pharmacotherapy and behavior therapy for persistent insomnia. *Am J Psychiatry*. 2002 Jan;159(1):5-11. PMID: 11772681.
 - b. Perlis M, Aloia M, Millikan A, Boehmler J, Smith M, Greenblatt D, Giles D. Behavioral treatment of insomnia: a clinical case series study. *J Behav Med*. 2000. Apr;23(2):149-61. PMID: 10833677.
 - c. Stepanski EJ, Perlis ML. Behavioral sleep medicine. An emerging subspecialty in health psychology and sleep medicine. *J Psychosom Res*. 2000 Nov;49(5):343-7. PMID: 11164058.
 - d. Perlis ML and Smith MT. How can we make CBT-I and other BSM services widely available? *J Clin Sleep Med*. 15; 4(1): 11–13. 2008.
4. **Advanced the effort to define insomnia as a disorder (as opposed to a symptom), particularly with respect to depression.** While many contributed to this effort, our contributions were to provide evidence that insomnia is a prodromal sign of (if not a triggering factor for) recurrent depression, to add to the burgeoning literature on insomnia as a risk factor for new onset unipolar depression, to add to the literature on insomnia as a risk factor for non-remission, and to be amongst three groups to articulate the argument that insomnia is best conceived of as comorbid disorder of depression.
- a. Perlis ML, Giles DE, Buysse DJ, Tu X, Kupfer DJ. Self-reported sleep disturbance as a prodromal symptom in recurrent depression. *J Affect Disord*. 1997 Feb;42(2-3):209-12. PMID: 9105962.
 - b. Perlis ML, Smith LJ, Lyness JM, Matteson SR, Pigeon WR, Jungquist CR, Tu X. Insomnia as a risk factor for onset of depression in the elderly. *Behav Sleep Med*. 2006;4(2):104-13. PMID: 16579719.
 - c. Pigeon WR, et. al. (Perlis Sr. Author). Is insomnia a perpetuating factor for late-life depression in the IMPACT cohort? *Sleep*. 2008 Apr;31(4):481-8. PMID: 18457235
 - d. Pigeon W, Perlis ML. Insomnia and Depression: Birds of a feather? *Int. J. Sleep Dis*. 1(3); 82-91. 2007.
5. **Conducted two of the first demonstrations that insomnia symptoms (incidence) occur in a predictable manner and collaborated on two of the first studies regarding the natural history of insomnia.** The demonstration of the non-randomness of symptom presentation in insomnia is important for at least two reasons. First, it suggests that homeostatic dysregulation contributes insomnia and in a manner that is predicted by several theoretical models including the Behavioral Model of Insomnia (the deleterious effects of sleep extension) and the Two Process Model (sleep extension contributes to a de-priming of “the” sleep homeostat). Second, it provides evidence for the hypothesis that placebo effects in insomnia occur as an interaction between pill use and the natural periodicity of illness severity (see below). The natural history studies are aimed at differentiating (and evaluating the transitions) between acute and chronic insomnia.
- a. Perlis ML, Zee J, Swinkels C, Kloss J, Morgan K, David B, Morales K. The incidence and temporal patterning of insomnia: a second study. *J Sleep Res*. 2014. Oct;23(5):499-507. PMID:24730977

- b. Perlis ML, Swinkels CM, Gehrman PR, Pigeon WR, Matteson-Rusby SE, Jungquist CR. The incidence and temporal patterning of insomnia: a pilot study. *J Sleep Res.* 2010 Mar;19(1 Pt 1):31-5. PMID: 19912510.
 - c. Perlis M, Gehrman P and Ellis J. The Natural History of Insomnia: What We Know, Don't Know, and Need to Know. *Sleep Medicine Research.*2012. 2(3): 79-88.
 - d. Ellis JG, Perlis ML, Neale LF, Espie CA, Bastien CH. The natural history of insomnia: Focus on prevalence and incidence of acute insomnia. *J Psychiatr Res.* 2012 Jul 14. PMID: 22800714.
6. **Contributed to the literature regarding sleep and suicide.** Our research focus is on the possibility that being awake at night confers increased risk for suicide and that this may be so owing to circadian and homeostatic effects on frontal lobe activity and executive function. Our collaborative work in this area is summarized in the following publications.
- a. Perlis M, Grandner M, Brown G, Basner M, Chakravorty S, Morales K, Gehrman P, Chaudhary N, Dinges D. Nocturnal Wakefulness: A Previously Unrecognized Risk Factor for Suicide. (In submission).
 - b. Bernert RA, Kim JS, Iwata NG, Perlis ML. Sleep disturbances as an evidence-based suicide risk factor. *Curr Psychiatry Rep.* 2015 Mar;17(3):554. PMID: 25698339.
 - c. Chakravorty S, Grandner MA, Mavandadi S, Perlis ML, Sturgis EB, Oslin DW. Suicidal ideation in veterans misusing alcohol: relationships with insomnia symptoms and sleep duration. *Addict Behav.* 2014 Feb;39(2):399-405. PMID: 24169371.
 - d. Smith MT, Perlis ML, Haythornthwaite JA. Suicidal ideation in outpatients with chronic musculoskeletal pain: an exploratory study of the role of sleep onset insomnia and pain intensity. *Clin J Pain.* 2004 Mar-Apr;20(2):111-8. PMID: 14770051.
7. **Contributed to the conceptualization of how and why placebo effects occur as they do in insomnia.** To date our contribution to this arena has been one theoretical paper and two follow-up empirical studies. The theoretical paper made the point that "something is reinforcing expectancy and it may well be the co-occurrence of placebo use with the periodic improvements that appear to occur regularly in chronic insomnia. The theory paper is below. The empirical papers are above (PMID: 24730977 & PMID: 19912510). Our other main contribution to this work is on-going and involves our NIH funded study on partial reinforcement as method for maintaining treatment response over time. This paper is in submission and is summarized in text.
- a. Perlis ML, McCall WV, Jungquist CR, Pigeon WR, Matteson SE. Placebo effects in primary insomnia. *Sleep Med Rev.* 2005 Oct;9(5):381-9. Review. PubMed PMID: 16109495.

Complete list of published work available at:
<http://www.ncbi.nlm.nih.gov/pubmed/?term=Perlis+M>

D. Research Support

CURRENT RESEARCH SUPPORT

4-R01AG041783-04 (Perlis)	07/01/13-05/31/17	4.2 cal months
NIH/NIA	\$301,708	

Prospective Assessment of the Etiology of Insomnia in Middle Aged & Elder Adults

Goal/Aim: To evaluate the factors that mediate/moderate the transitions from: Good Sleep to Acute Insomnia; Acute Insomnia to Good Sleep (recovery); and from Acute Insomnia to Chronic Insomnia.

1R56AG050620 (Perlis)	09/30/16-08/31/17	3.6 Calendar
NIH/NIA	\$400,024	

Three Approaches to Maintenance Therapy for Chronic Insomnia in Older Adults

This study evaluates whether one or both of two low frequency partial reinforcement (PR) strategies may be used for maintenance therapy with hypnotics. The two low frequency PR strategies will be compared nightly and intermittent dosing on several treatment outcome measures (i.e., relapse rates and average sleep continuity values in subjects that are non-relapsers). The groups will also be compared on the incidence and severity of side effects and adverse events. This data will be used to support a re-submission of the parent R01.

R21 HD 083628- 01-A1 (Perlis/Kloss) 09/23/15 – 08/31/17 1.8 cal months
NIH \$180,499

Natural History of Sleep Disturbance in Childbearing Women: A Feasibility Study

This study is designed to assess how sleep disturbance is expressed across pregnancy (from pre-pregnancy to post-partum) and to further evaluate what symptoms reach criteria for diagnosable disorders and/or are associated with adverse fetal or maternal outcomes

PENDING

1K24AG055602-01 (Perlis) 04/01/17-03/31/22 6.0 cal mos
NIA \$157,904

This award has two training foci (one for Dr. Perlis and one for his students) and a research component. The research component entails the establishment of a collaborative network of Jr. Investigators to conduct archival analysis using Dr. Perlis' NIA supported natural history of insomnia databases (R01AG041783). Ten Jr. Investigators, seven of whom are present or former trainees of Dr. Perlis, will bring their specialized expertise to the analysis of this rich data set. The cleaned and de-identified data set will be opened to the group during the first year of the K24 award (2017) and all the proposed archival analysis will be completed by the end of the following year (2018). The NHI data set is sufficiently comprehensive to allow for a host of post hoc analysis including (but not limited to): 1) an examination of the potential factor structure of the Insomnia Severity Index and their association with state change; 2) an evaluation of the use of alcohol relative to sleep disturbance and whether such use is associated with the final status of subjects with respect to insomnia; 3) the prospective assessment of sleep disturbance with new onset cancer, chronic pain and infertility. As a culmination of these activities, a small conference will be convened where all 10 investigators will be provided honoraria to come to Penn to present and discuss their findings.

Overlap: none

RECENTLY COMPLETED RESEARCH SUPPORT (within last 5 years)

Merck 818592 (Gehrman) 09/01/13-08/31/15 0.6 cal months
Merck and Co., Inc \$112,090

Metabolomics of Insomnia-related Hyperarousal

Goal/Aim: The goal of this study is to identify metabolic processes involved in the pathophysiology of insomnia.
Role: Co-I

R21MH076855 (Matteson) 2008-2010

Information Processing at Sleep Onset and During Sleep in Patients with Insomnia

Goal/Aim: To describe evoked response potential differences (i.e., information processing differences) in good sleepers as compared to patients with chronic insomnia.

58077-LS-DRP (Bhatnagar) 12/1/11-11/30/13
DoD/DARPA

Novel Approaches to Preventing the Effects of Stress

Goal/Aim: To determine the impact of traumatic stress on neurobiological measures of hyperarousal

5R01AT003332-05 (Perlis) 09/30/06-08/31/13

NIH/NCCAM

The Role of Partial Reinforcement in the Long Term Management of Insomnia

Goal/Aim: To determine if placebos may function as conditioned stimuli for pharmacotherapeutic effects.

R01CA126968 (Roscoe) 2/01/08 -1/31/14

NIH/NCI

CBT +/- Modafinil for Insomnia and Fatigue following Chemotherapy

Goal/Aim: To evaluate the effects of CBT-I, alone or in combination with modafinil, in cancer survivors with insomnia and fatigue.

5R01MH077900-04 (Perlis)

07/03/08 -03/31/14

NIH/NIMH

Attention Bias as an Etiologic Factor in Primary and Secondary Insomnia

Goal/Aim: To assess the relative contribution of attention bias and cortical arousal to insomnia severity in patients with Primary Insomnia, Insomnia co-morbid with acute MDD and Insomnia co-morbid with remitted MDD.

R34HL109462 (Gooneratne)

08/15/12-05/31/15

NIH/NHLBI

\$150,000

Understanding the sleep apnea/insomnia interaction: a CPAP/sham-CPAP trial

Goal/Aim: To assess to what extent CPAP treatment ameliorates sleep initiation and maintenance difficulties

Role: Co-I