BIOGRAPHICAL SKETCH

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NAME: William Paul Nobis

eRA COMMONS USER NAME (credential, e.g., agency login): NOBISWP

POSITION TITLE: Assistant Professor

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Michigan State University	B.S.	05/2004	Biochemistry
Vanderbilt University	Ph.D.	09/2009	Neuroscience
Vanderbilt University School of Medicine	M.D.	05/2011	Medicine
Northwestern University - Internal Medicine	Internship	06/2012	Internal Medicine
Northwestern University - Adult Neurology Residency	Residency	06/2015	Adult Neurology
Northwestern University - Adult Epilepsy Fellowship	Fellowship	06/2017	Adult Epilepsy

A. Personal Statement

I am a graduate of the M.D./Ph.D. program at Vanderbilt University, studying neuronal alterations similar to those thought to form the basis for learning and memory that also occur after drug exposure in the lab of Dr. Danny Winder. We discovered a direct and rapid interaction between dopamine and adrenergic systems (reward and stress systems of the brain) to activate the release of the neuropeptide corticotrophin-releasing factor and regulate excitatory glutamatergic transmission and plasticity in a brain region, the extended amygdala, key to reinstatement of drug-seeking behavior; these studies were conducted with electrophysiological methods to measure glutamatergic transmission and synaptic plasticity. During my 3.5 years of graduate work, I published two first-author on my thesis work.

I continued my training as a resident in Neurology and Epilepsy at Northwestern University where I broadened my exposure in neuroscience but remained fascinated by these brain regions and their potential unexplored role in epilepsy. I performed a research fellowship with Dr. Geoffrey Swanson where I learned detailed hippocampal anatomy and electrophysiological study of hilar mossy cells and hippocampal plasticity. My independent research interests lie on the most common cause of mortality in epilepsy, sudden unexplained death in epilepsy (SUDEP), bringing the bedside observation that stimulation of the extended amygdala produces apnea to the bench to examine the role of this brain region in seizures and respiratory control. This training path takes advantage of my unique training and exposure to these brain regions involved in the stress axis that are also intimately associated with respiration as well as my expertise in electrophysiology, and clinical training in neurology, epilepsy, and electroencephalogram (EEG). I hope that my translational and basic science explorations will be broadly applicable to sudden death via neurologic mechanisms including SUDEP, neurodegenerative diseases, respiratory dysfunction in seizures, and sudden infant death.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2020 - Present Assistant Professor, Department of Neurology at Vanderbilt University Medical Center
2018 - 2020 Clinical Instructor, Department of Neurology at Vanderbilt University Medical
2017 - 2018 Clinical Instructor, Department of Neurology and Clinical Neurological Sciences at

	Northwestern University's Feinberg School of Medicine Center
2015 - 2017	Adult Epilepsy Fellow, Department of Neurology and Clinical Neurological Sciences at Northwestern University's Feinberg School of Medicine ABPN board certification in Epilepsy completed 10/2018
2012 - 2015	Adult Neurology Resident, Department of Neurology and Clinical Neurological Sciences at Northwestern University's Feinberg School of Medicine ABPN board certification completed 9/2015
2011 - 2012	Internal Medicine Preliminary Year Internship, Northwestern University

Professional Memberships
Physicians for a National Health Program (PNHP)
Society for Neuroscience (SFN)
American Epilepsy Society (AES)
American Academy of Neurology (AAN)
American Clinical Neurophysiology Society (ACNS)

Honors

2000 - 2004	Gary L. Seevers Scholarship, Michigan State University Honors College
2002 - 2004	Howard Hughes Undergraduate Research Scholar
2008, 2009	Best Poster, Vanderbilt Brain Institute Annual Neuroscience Retreat
2013, 2014	Medical Student Teaching Award, Neurology Residency
2014	Chief Resident Northwestern Neurology Residency
2014	"Champagne Bottle" award for 90th percentile on neurology in-service exam
2015	AAN Enhanced Resident Leadership Program
2017	AES Young Investigator Award
2020	ACNS Young Investigator Award

C. Contributions to Science

Sudden Unexpected Death in Epilepsy (SUDEP)

I have two publications that contribute to the emerging literature on respiratory control and the amygdala with potential implications for the pathophysiology of SUDEP – detailing the role of the amygdala in breathing and the effect of seizure involvement in the amygdala on apneas. This has formed the basis for my research program and focus on the forebrain connections that may be involved in apneas and hypoventilation related to seizures. To that end, I have a detailed electrophysiological dissection of an extended amygdalar nucleus and it's connections to brainstem circuits in an epilepsy and SUDEP model recently published in *eNeuro*. Finally, I have a high-profile case report of a near SUDEP that illustrates the effects of amygdala involvement and hypoventilation may play in this entity. Overall, these publications form the clinical and translational basis for my basic science research.

1. **Nobis WP**, Schuele S, Templer JW, Zhou G, Lane G, Rosenow JM, Zelano C. Amygdala stimulation-induced apnea is attention and nasal-breathing dependent. Annals of Neurology*, February.* PMCID: PMC5867259
2. **Nobis WP**, Oturula-Gonzalez K, Templer JW, Gerard EE, Lane G, Rosenow JM, Zelano C, Schuele S. The effect of seizure spread to the amygdala on respiration and onset of ictal central apnea. Journal of Neurosurgery. 2019 April. PMCID: 30952127
3. Johnson M, Samudra N, Gallagher MJ, Abou-Khalil B, **Nobis WP**. Near SUDEP during bilateral stereo-EEG monitoring characterized by diffuse postictal EEG suppression. 2021 April. PMCID: 33617691
4. Yan WW*, Xia M*, Levitt A, Hawkins N, Kearney J, Swanson GT, Chetkovich DM, **Nobis WP.** Enhanced synaptic transmission in the extended amygdala and altered excitability in an extended amygdala to brainstem circuit in a dravet syndrome mouse model. eNeuro 2021; PMCID: 8213443

Epileptogenesis

Since the completion of my neurology residency and epilepsy fellowship I have been dedicated to epilepsy research, beginning with classic hippocampal circuits and epileptogenesis. The publication in *eNeuro* while in the Swanson laboratory fills a knowledge gap in hippocampal circuitry and highlights how the back-projection from CA3 to hilar mossy cells might contribute to hippocampal network hyperexcitability and cell death in

epilepsy. Additionally, more recently I have worked with my consultants at Vanderbilt to continue a dissection of hippocampal circuits, working with Dr. Harrison on an Alzheimer's disease model exploring the role of epileptogenesis and decline in cognition in a recently published manuscript in *Neurobiology of Disease*.

1. Hedrick TP*, **Nobis WP***, Foote KM, Ishii T, Chetkovich DM, Swanson GT. Excitatory synaptic input to hilar mossy cells under basal and hyperexcitable conditions. eNeuro. 2017 *4 (6).* PMCID: PMC5714709
2. Wilcox, Consli, Tienda, Dixit, **Nobis WP****,Harrison F**. Altered synaptic glutamate homeostasis contributes to cognitive decline in young APP/PSEN1 mice. Neurobiology of Disease 2021; PMCID: 34450329

Interactions between monoaminergic systems and corticotrophin releasing factor in the BNST

During my graduate work I studied the bed nucleus of the stria terminalis (BNST) in the laboratory of Dr. Danny Winder. The BNST is a component of the extended amygdala that extends anatomically between reward and stress centers and is involved in many physiological and behavioral functions including modulation of stress, anxiety, and relapse to drug seeking. I discovered that not only does dopamine increase excitatory glutamate signaling in this brain region but that it surprisingly also required the neuropeptide corticotrophin-releasing factor (CRF) to act. This work was extended in a further paper to investigate the relationship between noradrenergic signaling and CRF signaling within the BNST. Interestingly the action of norepinephrine and CRF on excitatory transmission was disrupted by repeated cocaine administration. These findings present a potential cellular mechanism for behavioral reinstatement data in the BNST and an important new target to consider for therapeutics that might address stress-induced relapse.

1. **Nobis WP***, Kash TL*, Silberman Y, Winder DG. Beta-adrenergic receptors enhance excitatory transmission in the bed nucleus of the stria terminalis through a corticotrophin-releasing factor receptor-dependent and cocaine-regulated mechanism. Biological Psychiatry. 2011 Jun 1;69(11):1083-90. PMCID: PMC3090515
2. Kash TL*, **Nobis WP***, Matthews RT, Winder DG. Dopamine enhances fast excitatory synaptic transmission in the extended amygdala by a CRF-R1-dependent process. The Journal of Neuroscience. 2008 Dec; 28(51): 13856-65. PMCID: PMC2630395
3. McElligott ZA, Klug JR, **Nobis WP**, Patel S, Grueter BA, Kash TL, Winder DG. Distinct forms of Gq-receptor-dependent plasticity of excitatory transmission in the BNST are differentially affected by stress. Proceedings of the National Academy of Sciences of the United States of America. 2010 Feb; 107(5): 2271-6. PMCID: PMC2836642

A full list of published works can be found at:
https://www.ncbi.nlm.nih.gov/myncbi/william.nobis.1/bibliography/public/
*denotes authors contributed equally to these works. **denotes co-corresponding authors

Research Support

Ongoing and recently completed relevant research support

Vanderbilt Faculty Research Scholars Award 7/1/2019-6/30/2022
Role: PI

American Epilepsy Society Junior Investigator Award 8/1/2019-12/31/2020
Epilepsy Foundation
The role of the extended amygdala in respiratory control and SUDEP.
Role: PI

1R01ES031401-01 2/1/2020 - 10/31/2024
NIH, National Institute of Environmental Health Sciences
Manganese exposure susceptibility as a modifier of excitotoxicity in Alzheimer's Disease
Role: Collaborator

Center for SUDEP Research, Pilot Grant 9/1/18-8/31/19
NINDS Center for SUDEP Research (CSR)
Role: PI