OMB No. 0925-0001 and 0925-0002 (Rev. 12/2020 Approved Through 02/28/2023)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
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NAME: J. Thomas Cunningham, Ph.D

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

POSITION TITLE: Regents Professor, Department of Physiology and Anatomy and Associate Dean for Research, Graduate School of Biomedical Sciences

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 DateMM/YYYY | FIELD OF STUDY |
| --- | --- | --- | --- |
| Eastern Illinois University | BA | 05/1982 | Psychology |
| University of Iowa | MA | 05/1984 | Biopsychology |
| University of Iowa | PhD | 08/1988 | Biopsychology |
| McGill University | Postdoctoral | 10/1990 | Neuroscience |
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**A. Personal Statement**

Our laboratory studies the role of the central nervous system in body fluid homeostasis and blood pressure regulation. We have conducted this type of research with continuous funding from NIH since 1995. Our longterm goal is to determine how changes in CNS network function contribute to chronic pathophysiological states. We perform experiments using animal models of cardiovascular disease to investigate the role of the central nervous system in states of chronic sympathetic activation using radio telemetry and chronic instrumentation to deliver pharmacological tools such as viral vectors with dominant negative constructs or shRNA to regions of the nervous system. These approaches are used in combination with functional euroanatomical techniques, such as Fos and ΔFosB immunohistochemistry, to obtain a better understanding of the CNS networks that regulate autonomic function. In addition, approaches such as brain slice electrophysiology, calcium imaging and laser capture microdissection are employed to better determine mechanisms on the cellular level. We have also developed more current techniques such as site specific optogenetic stimulation to complement our in vivo and in vitro experiments. Our laboratory studies the central control of vasopressin release to define osmotic and nonosmotic regulatory mechanisms that contribute to the physiological control of body fluid balance during physiological challenges and pathophysiological states. We also study the role of the central nervous system in animal models of hypertension. Recently, this research program has focused on a model of hypertension related to the intermittent hypoxemia associated with sleep apnea. Our laboratory is committed to the training of graduate, undergraduate students and professional students as well as postdoctoral fellows who are interested in traditional and non-traditional careers in the biomedical sciences.

Ongoing projects that I would like to highlight include:

R01 HL155977

Cunningham, J.T. (PI)
01/18/2021-12/31/2024

Intermittent Hypoxia and Hypertension: Role on the Lamina Terminalis

R01 HL142341

Cunningham, J.T. (PI)
04/15/2018-03/31/2022

Neural Regulation of Vasopressin Release in a model of Dilutional Hyponatremia

Citations:

1. Farmer GE, Amune A, Bachelor ME, Duong P, Yuan JP, Cunningham JT. Sniffer cells for the detection of neural angiotensin ii in vitro. *Scientific reports*. 2019;9:8820. PMCID: PMC6584535
2. Marciante AB, Wang LA, Farmer GE, Cunningham JT. Selectively inhibiting the median preoptic nucleus attenuates angiotensin ii and hyperosmotic-induced drinking behavior and vasopressin release in adult male rats. *eNeuro*. 2019;6 PMCID: PMC6437658
3. Snyder B, Shell B, Cunningham JT, Cunningham RL. Chronic intermittent hypoxia induces oxidative stress and inflammation in brain regions associated with early-stage neurodegeneration. *Physiological reports*. 2017;5 PMCID: PMC5430123

**B. Positions, Scientific Appointments, and Honors**

**Positions and Scientific Appointments**

2019-2020 Interim Chair, Department of Physiology and Anatomy, University of North Texas Health Science Center at Fort Worth

2018-2019 Interim Dean, Graduate School of Biomedical Sciences, University of North Texas Health

Science Center at Fort Worth.

2018-Present Associate Dean for Research, Graduate School of Biomedical Sciences, University of North

Texas Health Science Center at Fort Worth.

2016-Present Regents Professor, Department of Physiology and Anatomy, University of North Texas Health

Science Center at Fort Worth.

2009-2015 Director, Cardiovascular Research Institute, University of North Texas Health Science Center

at Fort Worth.

2009-2016 Professor, Department of Integrative Physiology, University of North Texas Health Science

Center at Fort Worth.

2003-2009 Associate Professor, Department of Pharmacology, University of Texas Health Sciences

Center at San Antonio.

2001-2003 Associate Professor with Tenure, Department of Physiology and the Dalton Cardiovascular

Research Center, University of Missouri-Columbia.

1995-2001 Assistant Professor, Department of Physiology and the Dalton Cardiovascular Research

Center, University of Missouri-Columbia.

1994-1995 Assistant Research Scientist, F.M. Abboud, M.D. Department of Internal Medicine and the

Cardiovascular Center, University of Iowa.

1992-1994 Research Fellow, F.M. Abboud, M.D. & S.J. Lewis; Department of Internal Medicine and the

Cardiovascular Center, University of Iowa.

1990-1992 Postdoctoral Fellow; L.P. Renaud, M.D. Ph.D.; Neuroscience Unit, Division of Neurology,

Ottawa Civic Hospital and the University of Ottawa.

**Honors**

2018 Lenard Share Award of the APS Water & Electrolyte Homeostasis Section

2017 Outstanding Graduate Faculty Member, UNT Health Science Center

2017-Present Editorial Board *Journal of Neuroendocrinology*

2017-2019 Chair, NNRS study section, NIH CSR

2015-2017 Regular Member/Stand in Chair, NNRS study section, NIH CSR

2014-Present Consulting Editor, *American Journal of Physiology: Regulatory, and Comparative Physiology*

2013-2014 Chair of AHA Cardiorenal 3 Study Section

2013 Star Reviewer for American Journal of Physiology: Regulatory, Integrative and Comparative

Physiology

2013 Presidents Award for Excellence in Research, UNT Health Science Center.

2013 Golden Apple Teaching Award, Graduate School of Biomedical Sciences, UNT Health

Science Center

2001-2012 Editorial Board for Experimental Neurology

2001-Present Editorial Board for Hypertension

2000-2001 Editorial Board for American Journal of Physiology: Heart and Circulatory Physiology.

2000 Dorsett L. Spurgeon MD, Distinguished Medical Research Award, University of Missouri-

Columbia School of Medicine

1999-2021 Editorial Board for American Journal of Physiology: Regulatory, Integrative and Comparative

Physiology

1999 American Physiological Society Young Investigator Award in Regulatory and Integrative

Physiology

1998 Award for Excellence in Preclinical Medical Education, University of Missouri-Columbia

**C. Contributions to Science**

1. Nonosmotic control of vasopressin release.

Nonosmotic control of vasopressin release is important to the development of hyponatremia associated with heart and liver failure. However, our understanding of these mechanisms is still incomplete. Beginning in the 1990’s, our work has used in vivo electrophysiology and functional neuroanatomical approaches to identify the central pathways that contribute to the cardiovascular regulation of vasopressin release. This work leads to a recent publication demonstrating that chronic salt loading produces changes in GABAergic neurotransmission that converts baroreceptor inhibition of vasopressin neurons into excitation. This is a novel form of plasticity mediated by changes in chloride transporter function that may have broader implications for other neural networks.

* 1. Grindstaff RR, Grindstaff RJ, Cunningham JT (2000) Effects of right atrial distension on the activity of magnocellular neurons in the supraoptic nucleus. Am J Physiol Regul Integr Comp Physiol 278:R1605-R1615.
	2. Knight WD, Ji LL, Little JT, Cunningham JT (2010) Dehydration followed by sham rehydration contributes to reduced neuronal activation in vasopressinergic supraoptic neurons after water deprivation. American Journal of Physiology - Regulatory, Integrative and Comparative Physiology 299:R1232-R1240. PMCID: PMC2980450
	3. Choe KY, Han SY, Gaub P, Shell B, Voisin DL, Knapp BA, Barker PA, Brown CH, Cunningham JT, Bourque CW (2015) High Salt Intake Increases Blood Pressure via BDNFMediated Downregulation of KCC2 and Impaired Baroreflex Inhibition of Vasopressin Neurons. Neuron 85:549-560. PMCID: PMC4577058
	4. Marciante AB, Wang LA, Farmer GE, Cunningham JT (2019) Selectively Inhibiting the Median Preoptic Nucleus Attenuates Angiotensin II and Hyperosmotic-Induced Drinking Behavior and Vasopressin Release in Adult Male Rats. eNeuro 6. PMCID: PMC6437658
1. Central mechanisms contributing to SAIDH.

In this line of research, we extended our work on the neural control of vasopressin release to include a model of dilutional hyponatremia associated with liver failure. Our results suggest that changes in transient receptor potential channel expression may lead to changes in osmotic sensitivity associated with hyponatremia. In addition, we have shown that a transcription factor FosB may contribute changes in gene expression that are necessary for the development of dilutional hyponatremia. The results of these studies will hopefully lead to a better understanding of changes in CNS network function that can contribute to pathophysiology and identify new treatment modalities or biomarkers for hyponatremia.

* 1. Carreno FR, Ji LL, Cunningham JT (2009) Altered central TRPV4 expression and lipid raft association related to inappropriate vasopressin secretion in cirrhotic rats. American Journal of Physiology-Regulatory Integrative and Comparative Physiology 296:R454R466. PMCID: PMC2643982
	2. Nedungadi TP, Carreno FR, Walch JD, Bathina CS, Cunningham JT (2012) Region- specific changes in transient receptor potential vanilloid channel expression in the vasopressin magnocellular system in hepatic cirrhosis-induced hyponatraemia. J Neuroendocrinol 24:642-652. PMCID: PMC3314151
	3. Cunningham JT, Nedungadi TP, Walch JD, Nestler EJ, Gottlieb HB (2012) {Delta}FosB in the supraoptic nucleus contributes to hyponatremia in rats with cirrhosis. Am J Physiol Regul Integr Comp Physiol 303:R177 185. PMCID: PMC3404636
	4. Balapattabi K, Farmer GE, Knapp BA, Little JT, Bachelor M, Yuan JP & Cunningham JT. (2019). Effects of Salt Loading on Supraoptic Vasopressin Neurons Assessed by ClopHensorN Chloride Imaging. J Neuroendocrinol, e12752. PMCID: PMC7041405
1. Central control of autonomic function and hypertension.

Our laboratory was one of the first to pioneer the use of functional neuroanatomical techniques to test the role of the central nervous system in experimental models of hypertension and to identify autonomic regulatory pathways. This approach has been widely used by other laboratories and has expanded our understanding of how the CNS contributes to the pathophysiology of hypertension.

* 1. Li Q, Sullivan MJ, Dale WE, Hasser EM, Blaine EH, Cunningham JT (1998) Fos-like immunoreactivity in the medulla after acute and chronic angiotensin II infusion. J Pharmacol Exp Ther 284:1165-1173.
	2. Lohmeier TE, Lohmeier JR, Warren S, May PJ, Cunningham JT (2002) Sustained activation of the central baroreceptor pathway in angiotensin hypertension. Hypertension 39:550-556.
	3. Cunningham JT, Herrera-Rosales M, Martinez MA, Mifflin S (2007) Identification of active central nervous system sites in renal wrap hypertensive rats. Hypertension 49:653-658.
	4. Farmer GE, Amune A, Bachelor ME, Duong P, Yuan JP & Cunningham JT. (2019). Sniffer cells for the detection of neural Angiotensin II in vitro. *Scientific reports* **9,** 8820. PMCID: PMC6584535
1. Changes in central control of autonomic function and intermittent hypoxia.

Intermittent hypoxia is widely used to model the hypoxemia associated with sleep apnea that produces hypertension. Our laboratory has studied the role of the CNS in this form of high blood pressure. Our result has identified regions of the forebrain that selectively contribute to the sustain component of the hypertension that is analogous to diurnal hypertension is sleep apnea patients. We have also demonstrated that the transcription factor FosB and the central renin-angiotensin system contribute to the forebrain mechanisms that are responsible for this sustained hypertension.

* 1. \*Zhang WR, Carreno FR, Cunningham JT, Mifflin SW (2009) Chronic Sustained Hypoxia Enhances Both Evoked EPSCs and Norepinephrine Inhibition of Glutamatergic Afferent Inputs in the Nucleus of the Solitary Tract. Journal of Neuroscience 29:3093-3102. PMCID: PMC2885697
	2. \*Knight WD, Little JT, Carreno FR, Toney GM, Mifflin SW, Cunningham JT (2011) Chronic intermittent hypoxia increases blood pressure and expression of FosB/DeltaFosB in central autonomic regions. Am J Physiol Regul Integr Comp Physiol 301:R131-139. PMCID: PMC3129875
	3. Cunningham JT, Knight WD, Mifflin SW, Nestler EJ (2012) An essential role for DeltaFosB in the median preoptic nucleus in the sustained hypertensive effects of chronic intermittent hypoxia. Hypertension 60:179 187. PMCID: PMC3415378
	4. \*Shell B, Farmer GE, Nedungadi TP, Wang LA, Marciante AB, Snyder B, Cunningham RL, Cunningham JT (2019) Angiotensin type 1a receptors in the median preoptic nucleus support intermittent hypoxia-induced hypertension. Am J Physiol Regul Integr Comp Physiol 316:R651-R665. PMCID: PMC6589598

**Complete list of Published Work in My Bibliography**

<http://www.ncbi.nlm.nih.gov/sites/myncbi/j.cunningham.1/bibliography/40312142/public/>