BIOGRAPHICAL SKETCH

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NAME: Díaz-Ríos, Manuel E.

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

POSITION TITLE: Associate 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
University of Puerto Rico, Río Piedras campus	BS	1996	Biology
University of Puerto Rico, Medical Sciences campus	PhD	2003	Anatomy/Neurobiology
Cornell University	Postdoc	2003-06	Neurophysiology

A. Personal Statement

Since my introduction to scientific research as an undergraduate student more than 15 years ago, my fascination on how nature shapes and changes behavior has increased 100-fold. Specifically, the relationship between neural networks and the induction and control of a behavior has personally become a passion. I was very fortunate during my graduate (doctoral) training to work on and appreciate the vast contribution that large identifiable neurons and the networks they comprise have had on the understanding of motor behavior by working on the marine mollusk *Aplysia californica* under the mentorship of Professor Mark W. Miller (Univ. of Puerto Rico). During this time I started my formal training in neuroanatomy and neurophysiology while dissecting and performing electrophysiological experiments on *Aplysia*. I continued developing my training as a neurophysiologist and gained new knowledge on calcium imaging techniques as a postdoctoral fellow at Cornell University under the mentorship of Professor Ronald Harris-Warrick (Dept. of Neurobiology and Behavior) in collaboration with Professor Watt W. Webb (Dept. of Applied Physics and Engineering) where I studied locomotor behavior on a more clinically-relevant vertebrate model system (mouse spinal cord). Today, I can honestly say that I can attribute my scientific and academic approach, as well as my leadership style as a principal investigator, to the influence of these great mentors. Additionally, I was able to gain expertise in a range of methodological strategies and approaches, including neurophysiology, neuroanatomy, calcium imaging and molecular neurobiology.

I was hired to the department of Anatomy and Neurobiology at the University of Puerto Rico medical school in 2006 after 3 years as a post-doc at Cornell. Unfortunately, I arrived just after a severe financial crisis hit the United States and Puerto Rico which led to a significant delay in gaining access to my start-up funds (no significant support from 2006 to 2010). I focused my efforts on teaching and service (including community outreach initiatives which led to NSF funding for student support, see completed research support). This had a significant impact on my publication record but I have since published 4 publications within the last 4 years including two manuscripts which are currently in revision.

Currently our laboratory studies how does the thoracic spinal circuitry is organized and controls trunk-related movements in mammals. Additionally, we are interested in studying how does this network utilizes and processes sensory input in neonatal and adult mice. Studies regarding the control of movement in vertebrates have been mostly focused on limb-related neural circuits but the organization of trunk-related neural networks, important for the control of body posture/balance, have been largely unexplored. We use intracellular and extracellular recordings as well as calcium imaging to assess the basic organization of this spinal neural network and which are its component neurons. Identifying and characterizing the modular organization and neural components involved in trunk motor control and its interaction with limb-related networks and afferent inputs would provide fundamental information regarding sensory-motor integration relevant to mammals and other vertebrate systems. Additionally, these future studies will eventually be directed toward improving current rehabilitative

strategies, such as those following stroke or spinal cord injury (SCI) by including the process of regaining proper trunk stabilization and postural control, crucial factors for stability and propulsion during walking.

Finally, we are interested in the study of the cellular effects of caffeine and other adenosine receptor antagonists and agonists on the spinal lumbar network controlling locomotion using the neonatal mouse spinal cord. Adenosine receptor have been shown to be powerful regulators of dopaminergic and glutamatergic neurotransmission in brain regions but little information has been provided within the spinal circuits controlling locomotion. We want to understand the cellular mechanisms by which adenosine receptor antagonists and agonist modulates the firing properties of the spinal CPG network for locomotion since adenosine receptors have been related to the reduction of inflammation and neuroprotection after a SCI and other neurodegenerative diseases of the central nervous system.

B. Positions and Honors

Positions and Employment

1992 - 1994	Laboratory Assistant, Laboratory of Dr. Ned Fetcher, Department of Biology, Univ. of Puerto Rico, Rio Piedras campus, San Juan PR
1996 - 1997	Laboratory Assistant, Laboratory of Dr. Susan Corey, Department of Pharmacology, Univ. of Puerto Rico, Medical Sciences campus, San Juan, PR
1998 - 2003	Doctoral student, Laboratory of Dr. Mark W. Miller, Department of Anatomy and Neurobiology, Univ. of Puerto Rico, Institute of Neurobiology, San Juan PR
1999 - 2001	Assistant Instructor, Tropical Neuroethology Summer Course, Sponsored by NSF and the Univ. of Puerto Rico, San Juan, PR
2000	Teaching Assistant, Medical Neuroscience Course, Univ. of Puerto Rico, School of Medicine, San Juan, PR
2003 - 2006	Postdoctoral Fellow, Cornell University, NY
2006 - 2013	Assistant Professor, Dept. of Anatomy and Neurobiology, Univ. of Puerto Rico, School of Medicine, San Juan, PR
2013 - today	Associate Professor, Dept. of Anatomy and Neurobiology, Univ. of Puerto Rico, School of Medicine, San Juan, PR

Other Experience and Professional Memberships

1999 -	Society for Neuroscience
1999 -	New York Academy of Sciences
2006 -	Organizing Committee, Puerto Rico Neuroscience Meeting
2007 -	Sigma XI, The Scientific Research Society
2007 -2014	Mentor in the Neuroscience Scholars Program (NSP) – NIH NINDS
2008 - 2014	Mentor in program offered by the Society for Neuroscience's (SfN) Committee on Women in Neuroscience (C-WIN)
2008 -	Participant in **B**rain **A**wareness **W**eek (BAW) at the Univ. of Puerto Rico, Medical Sciences
2009 - 2015	Co-Principal investigator (Co-PI) – NSF Undergraduate Research and Mentoring (URM) Program, *Neural Circuits and Behavior*.
2010 -	National Science Foundation Grant reviewer – Activation Panel (Washington, DC)
2013 -	Associate Professor, Dept. of Anatomy and Neurobiology, Univ. of Puerto Rico, School of Medicine, San Juan, PR
2010 -	Reviewer for the following journals: Journal of Neurophysiology, BMC Medical Genetics, Pharmacological reports, Current Medicinal Chemistry, Life Sciences, Neuroscience Letters

Honors

2000	Recipient of the 1st Annual Society for Neuroscience Chapters Graduate Student Travel Award, 30th Annual Meeting for the Society of Neuroscience (New Orleans, LA)
2002	Fellow in the Summer Program in Neuroscience, Ethics and Survival (SPINES) at the Marine Biological Laboratory (Woods Hole, MA)
2001-2003	American Psychological Association (APA), Minority Fellowship Program (MFP) in Neuroscience Predoctoral Fellow (NIH)

2003-	Award for excellence in academics (Honor role) and research given by the Associated Deanship for Biomedical Sciences, Univ. of Puerto Rico, Medical Sciences Campus, School of Medicine, at 2003 School of Medicine graduation ceremony, Guaynabo, PR
2004-2005	American Psychological Association (APA), Diversity Program in Neuroscience Post-doctoral Fellow (NIH, NRSA)
2006	Invited speaker at the 32nd Annual East Coast Nerve Net at the Marine Biological Laboratory, Woods Hole, MA
2008	Invited presenter of poster entitled: "Serotonin Modulation of Intrinsic Properties of Ascending Ipsilateral interneurons in the Neonatal Mouse Spinal Cord" at the Christopher and Dana Reeve Foundation Spinal Cord Symposium, Atlanta (GA).
2011	Invited speaker at Emory University School of Medicine, Department of Physiology Seminar Series. "Walking Without a Brain: Assessing the Role of Sensory Input to Locomotor Behavior" (Atlanta, GA)
2013	Invited panelist at NSF-funded workshop: "How Organisms Walk the Tightrope Between Stability and Change". Cold Spring Harbor, NY.
2016	Participant of the Grass Foundation Neuroscience workshop at the Marine Biological Laboratory (MBL; Woods Hole, MA)

C. Contribution to Science

1. Anatomical and physiological characterization of feeding-related CPG neurons in *Aplysia californica*

My graduate studies focused on consummatory feeding behaviors in *Aplysia californica*, a marine mollusk whose patterns of motor activity are controlled by a polymorphic central pattern generator (CPG) circuit. Two key findings emerged regarding the localization and functional characterization of GABAergic and dopaminergic neurons within the feeding circuitry of *Aplysia*. First, using retrograde tracing techniques combined with immunohistochemistry, we found that GABA and dopamine were colocalized within two interneurons, B20 and B65, which participate in configuring the functional output of the feeding CPG network. We then used intracellular sharp electrode recordings combined with pharmacological manipulations to show that dopamine mediates divergent (B20 interneuron to B16 and B8 motorneurons) and convergent (B20 and B65 interneurons to B8 motorneurons) rapid excitatory effects from these two influential feeding-related CPG neurons.

a) Díaz-Ríos M, Suess E, Miller MW. Localization of GABA-like immunoreactivity in the central nervous system of Aplysia californica. (1999) *J Comp Neurol* 413(2):255-70.
b) Díaz-Ríos M, Oyola E, Miller MW. Colocalization of gamma-aminobutyric acid-like immunoreactivity and catecholamines in the feeding network of Aplysia californica. (2002) *J Comp Neurol* 445(1):29-46.
c) Díaz-Ríos M., and Miller M.W. Rapid Dopaminergic Signaling by Interneurons that Contain Markers for catecholamines and GABA in the Feeding Circuitry of *Aplysia*. (2005) *J. Neurophysiol.* 93(4): 2142-56.
d) Díaz-Ríos M., and Miller M.W. Target-specific regulation of synaptic efficacy in the feeding central pattern generator of *Aplysia*: Potential substrates for behavioral plasticity? (2006) *Biol Bull.* 210:215-29.

2. The Role of Commissural Interneurons in the Mouse Spinal Locomotor CPG Network

During my postdoctoral studies in the laboratory of Ronald Harris-Warrick, I continued pursuing my interests in motor systems working with the neonatal mouse lumbar spinal cord through the use patch clamp recordings and two-photon calcium imaging**.** We found that the application of serotonin, a key neurotransmitter known to activate locomotor behavior in mammals, was found to differentially modulate the intrinsic membrane properties of lumbar commissural interneurons (CINs) based on the their axonal projections with some being rhythmically active during locomotor behaviors suggesting that they may play important roles in the coordination of left–right movements during locomotion. The cellular targets and mechanisms of 5-HT actions were relatively unknown thus we investigated the possible role of serotonin in modifying dendritic calcium currents, using a combination of two-photon microscopy and patch clamp recordings, in identified CINs in the upper lumbar region. Our studies found that 5-HT reduced calcium currents while enhancing cell excitability suggesting that the possible reduction in *I*Ca indirectly inhibits a calcium-activated potassium conductance to enhance CIN spiking.

a. Zhong G., Díaz-Ríos M. and Harris-Warrick R.M. Serotonin modulates the properties of ascending commissural interneurons in the neonatal mouse spinal cord. (2006) *J Neurophysiol.* 95(3):1545-55.
b. Zhong G., Díaz-Ríos M., and Harris-Warrick R.M. Intrinsic and functional differences among commissural interneurons in the central pattern generator for locomotion in the neonatal mouse. (2006) *J Neurosci* 26(24):6509-17.
c. Wilson J, Dombeck D, Díaz-Ríos M, Harris-Warrick RM. and Brownstone RM. Two-photon calcium imaging of network activity in XFP expressing neurons in the mouse. (2007) *J Neurophysiol.* 97(4):3118-25.
d. Díaz-Ríos M, Dombeck D, Webb WW, and Harris-Warrick RM. Serotonin modulates dendritic calcium influx in commissural interneurons in the mouse spinal locomotor network. (2007) *J Neurophysiol* 98(4):2157-67.

3. The Role of Neuromodulation and Sensory Input on Spinal Motor Network Function

We are currently interested in the sensory input and neuromodulation shapes the firing properties of neurons within the spinal neural network of mammals. We first used of a novel semi-intact preparation that included the thoracolumbar spinal cord connected to the hindlimbs of the neonatal mouse to assess the effects of sensory afferent feedback during early postnatal development. We found that removing sensory feedback coming from the hindlimbs by way of a lower lumbar transection or by ventral root denervation revealed a positive correlation in the ability of sensory input deprivation to disrupt ongoing locomotor activity on older versus younger animals. The differences in the motor responses as a function of age could be correlated with the loss of excitatory activity from sensory afferents. We are additionally assessing the effects of adenosine receptor antagonists (such as caffeine) and agonists on the function of lumbar network controlling locomotion. Our results support an indirect stimulant effect of caffeine on the lumbar spinal network controlling hindlimb locomotion through the inhibition of A1 adenosine receptors and subsequent activation of D1 dopamine receptors via a PKA-dependent intracellular mechanism. These effects have been recently linked to the presence of A1-D1 heteromers within spinal motoneurons and not interneurons within the lumbar spinal cord of mice. A_1-D_1 receptor heteromers play a significant control of the motoneuron excitability, represent main targets for the excitatory effects of caffeine in the spinal cord and can constitute a new target for the pharmacological therapy after spinal cord injury.

Finally, and in accordance with our laboratory mission of public outreach and service, we conducted a study with two psychologists measuring the prevalence and frequency of energy drink (ED) consumption among college students according to gender, degree programs and specific university-related and social situations. Additionally, we were interested in assessing the frequency of consumption of ED mixed with alcoholic beverages. We found that the majority of students consumed EDs occasionally and while studying. Also, we found a high consumption of EDs and of EDs mixed with alcohol by students in graduate programs which could be explained by a higher and more complex study load requiring longer periods of wakefulness and concentration. Future studies looking at the consumption patterns of EDs in more competitive graduate programs such as medical and/or dentistry school should be considered.

a. Acevedo J and Díaz-Ríos M. Lack of Sensory Input disrupts Spinal Locomotor Behavior in Early Postnatal Development. (2013) *J Comp Physiol A Neuroethol Sens Neural Behav Physiol* 199(12):1105-16.
b. Rivera-Oliver MS, and Díaz-Ríos M. The use of caffeine and other adenosine receptor antagonists and agonists to treat the onset and effects of known neurodegenerative diseases (Review). (2014) *Life Sci 101(1-2):1-9.*
c. Acevedo J, Santana-Almansa A, Matos-Vergara N, Marrero-Cordero LR, Cabezas-Bou E, and Díaz-Ríos M. (2016) Caffeine stimulates locomotor activity in the mammalian spinal cord via adenosine A1 receptor-dopamine D1 receptor interaction and PKA-dependent mechanisms. *Neuropharmacology* 101:490-505.
d. Cabezas-Bou E, De León-Arbucias J, Matos-Vergara N, Álvarez-Bagnarol Y, Ortega-Guzmán J, Narváez-Pérez K, Cruz-Bermúdez ND, Díaz-Ríos M. A Survey of Energy Drink Consumption Patterns Among College Students at a Mostly Hispanic University. *J Caffeine Res.* 2016 Dec 1;6(4):154-162.
e. Díaz-Ríos M, Guertin PA, Rivera-Oliver M. Neuromodulation of spinal locomotor networks in rodents. *Curr Pharm Des.* 2017;23(12):1741-1752
f. Marla Rivera-Oliver M, Moreno E, Álvarez-Bagnarol Y, Ayala-Álvarez C, Cruz-Reyes N, Molina-Castro GC, Canela EI, Clemens S, Ferré S, Casadó V, and Díaz-Ríos M. Adenosine A_1-Dopamine D_1 Receptor Heteromers Control the Excitability of the Spinal Motoneuron. *J Neurosci 26 Oct 2017; submitted.*
g. Ferré S, Quiroz C, Guitart X, Rea W, Seyedian A, Moreno E, Casadó-Anguera V, Díaz-Rios M, Casadó V, Clemens S, Allen RP, Earley CJ and García-Borreguero D. Adenosine Neurotransmission in Restless Legs Syndrome. *Frontiers in Neurosci* 30 Oct 2017*; Submitted.*

Complete list of publications in MyBibliography: https://www.ncbi.nlm.nih.gov/pubmed/?term=Diaz-Rios+M

D. Research Support
Ongoing Research Support:

NIH 1P20GM103642-01A1 Rosenthal (PD) 07/01/13 - 06/30/18 $11,416,375
Center for Neuroplasticity at the University of Puerto Rico
The University of Puerto Rico (UPR) Medical Sciences Campus proposes to establish a COBRE Center that will significantly strengthen the research infrastructure of the institution and that will impact biomedical investigation throughout the island.
Project title: "The Role of Sensory Input to Mammalian Locomotion after the Loss of Supraspinal Inputs"
Role: Subproject P.I.

NSF 1337284 Miller (PI) 01/01/14 - 12/31/18 $255,762
MRI: Acquisition of a Shared Laser Scanning Confocal Microscope at the Institute of Neurobiology
The main goal of this proposal is to acquire a state-of-the-art Laser Scanning Confocal Microscope (LSCM). This instrument overcomes obstacles that previously limited the detection and precise localization of fluorescent signals within nervous systems and other complex three-dimensional structures.
Role: Co-PI; no direct research support.

Completed Research Support:
DoD W911NF-07-R-002 Miller (PI) 09/01/07 – 08/31/09 $471,000
Expansion of Imaging Facilities at the Institute of Neurobiology
The main goal of this proposal was to upgrade the existing confocal imaging facility located in the Institute of Neurobiology (San Juan, PR), a facility that belongs to the University of Puerto (School of Medicine). Role: Co-PI; no direct research support.

Craig Nielsen Foundation 124554 Díaz-Ríos (PI) 07/01/09 – 11/30/11 $196,440
Sensory Information to Spinal Cord Interneurons after Injury
Our goal is to use the neonatal mouse spinal cord preparation to study how important sensory input to the spinal cord circuitry through sensory feedback after injury is to the physiological "well being" of spinal interneuronal populations. Role: PI

NSF 0923132 Lasalde-Dominicci (PI) 09/01/09 – 08/31/12 $255,762
MRI/Acquisition: Upgrading the Confocal Imaging Facility at the University of Puerto Rico to Enable Emission Fingerprinting
An upgrade of the Confocal Imaging Facility at University of Puerto Rico (CIF-UPR, www.cifupr.org) will enable fluorescence emission fingerprinting, an innovative method for the recording, analysis and separation of emission signals in multi-fluorescence imaging. Role: Co-PI; no direct research support.

NSF 0963179 Treistman (PI) 10/01/10 – 09/30/13 $800,000
Renovation of the Institute of Neurobiology, University of Puerto Rico
Funds are provided to correct significant deficiencies including 1) an antiquated air conditioning system and 2) an obsolete network cyberinfrastructure. The rejuvenation of the INB will significantly improve ongoing and planned research opportunities. Role: Co-PI; no direct research support.

NSF 1026061 Díaz-Ríos (PI) 09/01/10 – 01/31/14 $199,982
RIG: Identification of Pacemaker Neurons Controlling Locomotor Behavior
We will conduct a detailed and focused anatomical, physiological and biophysical characterization of the IIN population in order to identify the pacemaking kernel controlling locomotion in the mouse spinal cord. Role: PI

NSF 0932955 Miller (PI) 09/01/09 – 08/31/14 $603,000
URM: Mentoring program in neural circuits and behavior at the Univ. of Puerto Rico.
The major goal of this project is to establish a mentoring program in neurobiology for 16 undergraduate students at the University of Puerto Rico. Role: Co-PI; no direct research support.