BIOGRAPHICAL SKETCH

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NAME: McDonald, M. Danielle

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

POSITION TITLE: Professor of Marine Biology and Ecology

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
McMaster University	BSc	05/1996	Biology
McMaster University	PhD	09/2002	Animal Physiology
Rosenstiel School of Marine, Atmospheric, and Earth Science (Rosenstiel School), University of Miami	Postdoctoral Scientist	06/2004	Fish Physiology/ Molecular Biology
Rosenstiel School, University of Miami	Assistant Scientist	06/2006	Fish Physiology/ Molecular Biology

A. Personal Statement

I am a Professor of Marine Biology and Ecology and the Glassell Family Endowed Chair in Marine Biomedicine. My research is focused broadly on animal physiology and toxicology, and while I work on marine animals, many of my research projects have applicability to human health and disease, including work that I have done on oil toxicology and exposure effects of polycyclic aromatic hydrocarbons, serotonin dynamics, and whole animal responses to environmental stressors such as low oxygen (hypoxia). My research program to date has been funded predominantly by the National Science Foundation (NSF), but I have recently become the Scientific Director of the NIH-funded National Aplysia Resource, and, to that end, my current research serves to determine the response of the California sea hare, *Aplysia californica* “Aplysia” nervous tissue and heart to ischemia and reperfusion as the animal ages. Through this work, I hope to fill current gaps in knowledge regarding Aplysia physiology and develop new uses for the Nobel-prize winning Aplysia model in the study of cerebral and myocardial ischemia/reperfusion injury (IRI). I am trained in whole animal physiology, transport physiology, endocrinology, and molecular biology, and have extensive experience with delicate survival surgeries as well as in the use of both *in situ* and *in vitro* tissue preparations to answer physiological questions. I have mentored more than 95 undergraduate, graduate, postdoctoral fellows, scientists, and junior faculty. I am an award-winning teacher within the Marine Biology and Ecology Undergraduate Program, advise undergraduates in research within my laboratory, and have been an academic advisor for the Rosenstiel School Undergraduate Program for over a decade. At the graduate level, I have won multiple awards for graduate student mentorship and in my position as the Rosenstiel School Associate Dean of Research, I have developed programs to improve the mentorship of junior Rosenstiel School faculty.

Ongoing and recently completed projects that I would like to highlight include:

P40 2P40OD010952-29
M.D. McDonald (Project Lead)
03/21/2024 - 02/20/2029
National Resource for Aplysia: Applied Research

NSF IOS-1754550
M.D. McDonald (PI)

06/10/2018 - 05/31/2024
The serotonin transporter (SERT) and the control of circulating serotonin in teleost fish

Citations:

a. Amador MHB, **McDonald MD** (2018) The serotonin transporter (SERT) and non-selective transporters are involved in peripheral serotonin uptake in the Gulf toadfish, Opsanus beta. Am J Physiol doi:10.1152/ajpregu.00137.2018
b. Sebastiani J, Sabatelli A, **McDonald MD** (2022) Mild hypoxia exposure impacts peripheral serotonin uptake and degradation in Gulf toadfish, *Opsanus beta*. J Exp Biol 225 (13): jeb244064. doi: 10.1242/jeb.244064 (featured in Inside JEB)
c. Milton EM, Cartolano MC, **McDonald MD** (2023) A multi-targeted investigation of *Deepwater Horizon* crude oil exposure impacts on the marine teleost stress axis. Aquat Toxicol 257:106444. doi: 10.1016/j.aquatox.2023.106444
d. Kron N, Young B, Drown M, **McDonald MD** (2024) Long-read *de novo* genome assembly of Gulf toadfish, *Opsanus beta*. BMC Genomics 25: 871. doi: 10.1186/s12864-024-10747-8

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2024	Director, Glassell Family Center for Marine Biomedicine
2024	Scientific Director, National Aplysia Resource
2022-2023	Associate Dean of Research, Rosenstiel School, University of Miami
2018-present	Professor, Department of Marine Biology and Ecology (MBE), Rosenstiel School, University of Miami
2013-2017	Associate Professor, Rosenstiel School, MBE, University of Miami, USA
2006-2012	Assistant Professor, Rosenstiel School, Division of Marine Biology and Fisheries (MBF), University of Miami, USA

Honors

2016	Rosenstiel School Outstanding Mentor Award
2015/2016	University of Miami Graduate School Faculty Mentor of the Year
2015	Linda Farmer Marine Science Undergraduate Teaching Award
2006	Company of Biologists Traveling Fellowship
2004-2006	National Science and Engineering Research Council (NSERC) Post-Doctoral Fellowship
2001	Ontario Post-Graduate Scholarship
2000	Ontario Post-Graduate Scholarship

C. Contributions to Science

I. For more than a decade, I have worked to establish a greater understanding of the role of the neurochemical serotonin (5-HT; 5-hydroxytryptamine) within vertebrates and how its role has evolved in the animal kingdom. My early research focused on investigating the receptors that mediated 5-HT function within teleost fish. My lab has found consistencies in the roles of the 5-HT_{1A} and 5-HT_{2A} receptors between fish and mammals in controlling various physiological responses. We determined that, similar to mammals, the 5-HT_{1A} receptor is involved in regulating the glucocorticoid stress response, and both receptor subtypes are sensitive to increases in circulating stress hormone. The evolutionary continuity demonstrated between teleost fish and mammals with respect to 5-HT receptors illustrate that fish, of which there are > 30,000 species that exploit all sorts of different environments, could be used as alternative animal models for the study of human 5-HT receptors, the 5-HT_{1A} receptor being very important in the regulation of 5-HT synaptic activity and mental health. I served as the primary investigator on all these studies.

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a. Medeiros LR, Mager EM, Grosell M, **McDonald MD** (2010) The serotonin subtype 1A receptor regulates cortisol secretion in the Gulf toadfish, *Opsanus beta*. Gen Comp Endocrinol 168: 377-387

b. Frere AW, **McDonald MD** (2013) The effect of stress on gill basolateral membrane binding kinetics of 5-HT_2 receptor ligands: potential implications for urea excretion. J Exp Zool 319A: 237-248
c. Medeiros LR, **McDonald MD** (2013) Cortisol-mediated downregulation of the serotonin 1A receptor subtype in the Gulf toadfish, *Opsanus beta*. Comp Biochem Physiol 164A: 612-21
d. Medeiros LR, **McDonald MD** (2012) Elevated cortisol inhibits adrenocorticotropin hormone- and serotonin-stimulated cortisol secretion from the interrenal cells of the Gulf toadfish (*Opsanus beta*). Gen Comp Endocrinol 179: 414-420
e. Medeiros LR, Cartolano MC and **McDonald MD** (2014) Crowding stress attenuates serotonin 1A receptor-mediated secretion of corticotropin releasing factor and adrenocorticotropin hormone in the Gulf toadfish. J Comp Physiol 184B: 259-271

II. I have also worked to understand how 5-HT has evolved in the animal kingdom by investigating the transporters that facilitate 5-HT movement within teleost fish. In mammals, freely circulating 5-HT causes vasoconstriction of blood vessels, and, to control this response, 5-HT is taken up by blood platelets via the 5-HT transporter (SERT). In fish, 5-HT also causes vasoconstriction, but cells analogous to platelets do not take it up. My lab was the first to show that, instead of by platelets, the highest amount of SERT and SERT-mediated 5-HT uptake is by the fish heart with significant uptake by the gill, an analogous structure to the mammalian lung. We were also the first to reveal that, like mammals, dopamine and norepinephrine transporters play a role in the regulation of circulating 5-HT in teleost fish, illustrating the evolutionary continuity between fish and mammals with respect to monoamine regulation, which is important in mental health disorders such as major depression and anxiety. We have also revealed that uptake and degradation of 5-HT by the gill is upregulated in response to hypoxia, contributing to a reduction in circulating 5-HT and systemic vasodilation. This work provides insight on how 5-HT may have evolved in its function within the cardiovascular and respiratory systems and how 5-HT dynamics within the body can change in response to hypoxia – a condition that could be caused by heart or pulmonary disease. I served as the primary investigator on all these studies.

a. **McDonald MD**, Gilmour KM, Walsh PJ, Perry SF (2010) Cardiorespiratory reflexes in the gulf toadfish, Opsanus beta. Resp Physiol Neurobiol 170: 59-66
b. Amador MHB, **McDonald MD** (2018) Molecular and functional characterization of the Gulf toadfish serotonin transporter (SERT; SLC6A4). J Exp Biol 221: pii: jeb170928 doi: 10.1242/jeb170928 (short-listed for 2018 JEB Outstanding Paper Prize)
c. Amador MHB, **McDonald MD** (2018) The serotonin transporter (SERT) and non-selective transporters are involved in peripheral serotonin uptake in the Gulf toadfish, Opsanus beta. Am J Physiol doi:10.1152/ajpregu.00137.2018
d. Sebastiani J and **McDonald MD** (2021) The role of uptake and degradation in the regulation of peripheral serotonin dynamics in Gulf toadfish, *Opsanus beta* Comp Biochem Physiol 258A: 110980 doi: 10.1016/j.cbpa.2021.110980
e. Sebastiani J, Sabatelli A, **McDonald MD** (2022) Mild hypoxia exposure impacts peripheral serotonin uptake and degradation in Gulf toadfish, Opsanus beta. J Exp Biol 225 (13): jeb244064. doi: 10.1242/jeb.244064 (featured in Inside JEB)

II. Given the importance of SERT in the control of circulating 5-HT and within the cardiovascular and respiratory systems described above, I have investigated the cardiovascular and respiratory impacts of SERT inhibition by the selective 5-HT reuptake inhibitor (SSRI), fluoxetine, which is the active ingredient in a common antidepressant known as Prozac™. Work in my laboratory has shown that treatment with fluoxetine results in the attenuation of the cardiovascular response to hypoxia that may limit survival when in low oxygen. This work could be applied to human health and the understanding of potential negative interactions of SSRI use and those that suffer physiological hypoxia because of heart or lung disease. Furthermore, in humans there are reported connections between cardiovascular disease and depression that are not well understood. I served as the primary investigator on all these studies.

a. Morando MB, Medeiros LR, **McDonald MD** (2009) Fluoxetine treatment affects nitrogen waste excretion and osmoregulation in a marine teleost fish. Aquat Toxicol 95: 164-171
b. Panlilio JM, Marin S, Lobl MB, **McDonald MD** (2016) Treatment with the selective serotonin reuptake inhibitor, fluoxetine, attenuates the fish hypoxia response. Sci. Rep. 6: 31148 doi:10.1038/srep31148o.

c. **McDonald MD** (2017) An AOP analysis of selective serotonin reuptake inhibitors (SSRIs) for fish. Comp Physiol Biochem 197C: 19-31 doi: 10.1016/j.cbpc.2017.03.007
d. Amador MHB, Schauer KL, **McDonald MD** (2018) Does fluoxetine exposure affect hypoxia tolerance in the Gulf toadfish, *Opsanus beta*? Aquat Toxicol 199: 55-64. doi: 10.1016/j.aquatox.2018.03.023.

IV. Polycyclic aromatic hydrocarbons (PAHs) are carcinogenic compounds that can be found in the environment naturally after volcanoes and forest fires, but also after anthropogenic processes that involve fossil fuel combustion. Humans are exposed through inhalation and across the skin, with smokers and fire fighters being particularly at risk. In the marine environment, marine mammals (*i.e.*, bottlenose dolphin), fish, and other marine organisms were exposed to PAHs in the 2010 Deepwater Horizon oil spill. Reports of bottlenose dolphin after the spill indicated that they were suffering from a reduced glucocorticoid stress response, lower body condition, and in some cases, adrenal gland failure. My Gulf of Mexico Research Initiative (GoMRI)-funded work explored whether fish experienced the same impaired cortisol release, which is the main stress hormone, in response to PAH exposure. We used toadfish as a model for bottlenose dolphin to determine the toxic mechanism and assess the potential for recovery. We found that toadfish did experience a disruption in the glucocorticoid stress response, and like bottlenose dolphin, this disruption occurred at the level of the interrenal cells (analogous to the adrenal gland). Like findings in dolphin, the disturbance in toadfish was in the rate of cortisol secretion and was most likely at the level of the MC2R receptor. This work was used to lend insight to PAH impacts on bottlenose dolphin and given the similarities between fish, dolphins, and humans with respect to the glucocorticoid stress response (for example, all three organisms use cortisol as their main glucocorticoid), suggests that similar PAH impacts might be present in humans. I served as the primary investigator on all these studies.

a. Reddam A, Mager EM, Grosell M, **McDonald MD** (2017) The impact of acute PAH exposure on the toadfish glucocorticoid stress response. Aquatic Toxicol: 195: 89-96 doi: 10.1016/j.aquatox,2017.08.014
b. Alloy MM, Cartolano MC, Sundaram R, Plotnikova A, **McDonald MD** (2021) Exposure and recovery from environmentally relevant concentrations of waterborne polycyclic aromatic hydrocarbons from weathered Deepwater Horizon slick oil: impacts on liver and blood endpoints. Environ Toxicol Chem 40:1075-1086 doi: 10.1002/etc.4966
c. Cartolano MC, Alloy MM, Milton E, Plotnikova A, Mager EM, **McDonald MD** (2021) Exposure and recovery from environmentally relevant levels of waterborne PAHs from Deepwater Horizon oil: effects on the Gulf toadfish stress axis. Environ Toxicol Chem 40:1062-1074 doi: 10.1002/etc.4945
d. Milton EM, Cartolano MC, **McDonald MD** (2023) A multi-targeted investigation of *Deepwater Horizon* crude oil exposure impacts on the marine teleost stress axis. Aquat Toxicol 257:106444. doi: 10.1016/j.aquatox.2023.106444

For a full list of my publications see:
https://www.ncbi.nlm.nih.gov/myncbi/1fWuvpV0dApQf/bibliography/public/