Brain Chemistry Labs

A Non-profit Research Institute - Jackson, Wyoming

Response to the Army Corps of Engineers, July 2020
Supplemental Environmental Analysis on a Deviation to LORS to Address HABs
Cyanotoxin Analyses of Water Releases from Lake Okeechobee

The Brain Chemistry Labs

The Brain Chemistry Labs is an independent not-for-profit research institute located in Jackson Hole, Wyoming. Currently, we have five Ph.D. scientists on our core staff and anchor a consortium of 50 Ph.D.s and M.D.s from 28 institutions around the world. Our mission is to improve patient outcomes by discovering new treatments for progressive neurodegenerative illnesses. As part of this mission, we are involved in analyzing cyanobacterial toxins which are risk factors for progressive neurodegenerative diseases including Alzheimer's, ALS, and Parkinson's disease.

Monitoring Cyanotoxins in Florida

As part of the Brain Chemistry Labs mission, we have been monitoring cyanobacterial toxins released by the U.S. Army Corps of Engineers down the St. Lucie River and the Caloosahatchee. We have now published two papers on our analysis of the 2016 release and the 2018 release of these waters by the U.S. Army Corps of Engineers in internationally circulated, peer-reviewed journals, e.g. the *Water Policy* journal, which is published in London by the World Water Council, and *Neurotoxicity Research*, which is published by the Neurotoxicity Society in the United States. Both of these articles have been published as open access papers, and so can be freely downloaded by decision makers at the Army Corps of Engineers and interested members of the public using the following references:

Metcalf JS, Banack SA, Powell JT, Tymm FJ, Murch SJ, Brand LE, Cox PA. 2018. Public health responses to toxic cyanobacterial blooms: perspectives from the 2016 Florida event. *Water Policy* 20: 919-932. DOI: 10.2166/wp.2018.012

Metcalf JS, Banack SA, Wessel RA, Lester M, Pim JG, Cassani JR, Cox PA. 2020. Toxin Analysis of Freshwater Cyanobacterial and Marine Harmful Algal Blooms on the West Coast of Florida and Implications for Estuarine Environments. *Neurotoxicity Research* 18: 1-9. DOI: 10.1007/s12640-020-00248-3

Lake Okeechobee Waters & Cyanobacterial Blooms on Both Florida Coasts

In 2016 and 2018, we identified emergency releases of nutrient-rich and cyanobacterially-laden waters from Lake Okeechobee by the U.S. Army Corps of Engineers as major causes of cyanobacterial blooms along the east and west coasts of Florida, potentially exposing tens of thousands of Florida residents and visitors to dangerous cyanobacterial toxins. Some of the toxins we identified in these releases from Lake Okeechobee are known to produce acute toxic effects, while others are risk factors for chronic health issues.

Cyanobacterial Blooms Negatively Impact Human Health
The risk of harm from cyanobacterial blooms has been well established, with the link between cyanobacteria and toxicity having been known since the 1870's[1,2]. Animal deaths have been caused by cyanobacterial toxins: microcystins, nodularins, anatoxin-a, anatoxin-a(S), saxitoxins, and cylindrospermopsins[1,3-10]. Human illnesses have also been caused by microcystins, LPS, cylindrospermopsin[11-13], with human deaths having been linked to the cyanobacterial toxins: microcystins, cylindrospermopsins and saxitoxins[14-17].

Chronic exposures to cyanobacterial toxins have also been linked to serious illnesses throughout the world. Long term exposure to microcystins is considered to be a risk factor for primary liver cancer[18,19], particularly in China, where exposure to microcystin is believed to account for a significant increase in primary liver cancer in Haimen and Fusui, and hepatocellular carcinoma in southwest China.

Water Releases from Lake Okeechobee Exceeded International Standards
We found that emergency releases of Lake Okeechobee water by the U.S. Army Corps of Engineers down the St. Lucie River in 2016 exceeded international standards for recreational waters by 2,000-fold. As we noted in our analysis of the 2016 U.S. Army Corps of Engineers release from Lake Okeechobee, "The concentration of microcystins contained within this material was extremely high, orders of magnitude greater than the WHO Guideline Value for MC-LR in drinking water of 1 µg/l (WHO, 1998)[20] and 2,000 times higher than German recreational Guideline Values (Ibelings et al., 2014)[21]. As a result of the MC concentration contained within the bloom material, closure or restriction of access to the waters should have occurred rapidly, if not immediately, with continuous monitoring to determine potential adverse health effects. Given the likelihood of long-term hepatotoxic or carcinogenic consequences from the microcystin content, it may have been prudent for public health officials to offer assistance to households living on the banks of or near the St. Lucie River until the cyanobacterial bloom subsided."

Lake Okeechobee Water Releases Increased Risks of Primary Liver Cancer
The long-term consequences of the 2016 human exposures of Florida residents to cyanobacterial toxins may be serious. As we noted, "Based on microcystin content alone reported here, it is a reasonable prediction that the cohort of Florida State citizens exposed to the 2016 Florida cyanobacteria bloom incident, including children of underprivileged families that we witnessed picnicking, fishing, and swimming in cyanobacterially contaminated waters, may experience an increased lifetime risk of liver cancer and/or hepatic dysfunction requiring hospitalization or transplantation."

Long-term exposure to BMAA should be considered a risk factor for human neurodegenerative diseases[22-41]. Evidence for BMAA being a risk factor for progressive neurodegenerative brain diseases comes from replicated controlled experiments with ApoE4 homozygous vervets at the Behavioural Science Foundation facility on the island of St. Kitts in the West Indies. Vervets with chronic dietary exposure to BMAA develop the two neuropathological hallmarks of Alzheimer's disease in their brains, neurofibrillary tangles formed from misfolded tau, and β-amyloid plaques[34], and

neuropathological hallmarks of ALS, specifically, microglial activation along the spine and deposits of misfolded TDP-43, and FUS proteins[22]. Clusters of ALS patients are found around lakes with persistent cyanobacterial blooms[37,42-45]. Sufficient toxicological studies to determine "safe" concentrations of BMAA and exposure routes have not been performed.

Cyanobacterial Neurotoxins as Risk Factors for Brain Diseases

While our primary concern in the 2016 and 2018 emergency water releases by the U.S. Army Corps of Engineers down the St. Lucie River and the Caloosahatchee were the extraordinarily high levels of microcystin, a potent liver toxin, we did detect BMAA in the cyanobacterial samples. Even low levels of BMAA are of concern because BMAA is persistent in the environment[46-51], biomagnifies in the food chain[52-58], has long-lasting effects on marine, freshwater aquatic, and terrestrial organisms[25,59-63], can be passed along to offspring[64-68], and may be airborne in areas with persistent blooms[41,69,70]. BMAA has been found in the brains of beached dolphins, sharks and fish exposed to cyanobacterial blooms[42,56,71]. Isomers of BMAA co-occur and are also toxic[72,73]. We detected isomers of BMAA in the emergency water releases from Lake Okeechobee by the U.S. Army Corps of Engineers[46,48]; recent *in vitro* studies from Marquette University suggests that 2,4-DAB and particularly AEG may be even more neurotoxic that BMAA[72]. 2,4-DAB also has proven toxicity *in vivo*[73].

Bacteria & Cyanobacterial Blooms

Human health problems from exposure to cyanobacterial blooms may also include infection from cholera bacteria which are harbored within the bloom ecosystem, as has been suggested in Bangladesh where blooms have been found to serve as environmental reservoirs for *Vibrio cholerae*[74-76]. It is possible that other bacterial pathogens and even viruses may be harbored and dispersed by cyanobacterial blooms.

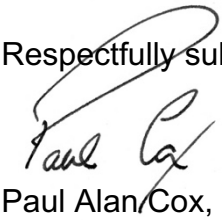
Health Impacts of Emergency Water Releases

We understand that the U.S. Army Corps of Engineers are charged with monitoring water levels in Lake Okeechobee so that breaching of the earthen dike which occurred in 1926 with a storm surge that resulted in 300 deaths, and two years later in 1928 during the San Felipe Segundo hurricane which caused thousands of fatalities downstream do not reoccur[77]. However, in making decisions on the timing of water releases from Lake Okeechobee, and interagency efforts to reduce nutrient inputs to the lake, the Corps might find it useful to consider potential health consequences associated with releases of nutrient-rich and cyanobacterially-laden waters down the Caloosahatchee and St. Lucie Rivers for coastal residents. Governments and institutions such as the World Health Organization have Guidelines concerning acceptable concentrations of cyanobacteria and cyanobacterial toxins in drinking, recreational and bathing waters and some countries have introduced legislation to protect human health[20,78]. The Army Corps of Engineers could use such guidelines to monitor lake waters and in the timing of releases to protect breaching of the dike.

This submission from the Brain Chemistry Labs was prepared in collaboration with Senior Scientist Dr. Sandra Banack, and Senior Researcher Dr. James Metcalf. The U.S. Army Corps of Engineers is welcome to contact any of us for further information on

what we have here reported. Our sole goal in responding is to help the Corps to protect the health of the residents of Florida.

Respectfully submitted,



Paul Alan Cox, Ph.D.
Executive Director

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Paul Alan Cox

Curriculum Vitae

Education

Ph.D. (Biology)	Harvard University	1981
A.M. (Biology)	Harvard University	1978
M.Sc. (Ecology)	University of Wales	1978
B.S. (Botany)	Brigham Young University	1976

Postdoctoral Experience

Miller Research Fellow, Miller Institute for Basic Research in Science	University of California, Berkeley	1981-1983
Melbourne Research Fellow	University of Melbourne	1985-1986

Academic Positions

Executive Director	Institute for Ethnomedicine	2005-
Executive Director	National Tropical Botanical Garden	1998-2004
Distinguished Professor	Brigham Young University–Hawaii	2000-2010
King Carl XVI Gustaf Professor of Environ. Sci.	Swedish Agricultural University	1997-
Dean of General Education & Honors	Brigham Young University	1993-1997
Professor	Brigham Young University	1991-1998
Associate Professor	Brigham Young University	1986-1991
Assistant Professor	Brigham Young University	1983-1986
Visiting Professor	Uppsala University	1990
Visiting Professor	Umeå University	1990

Adjunct Professorships

Visiting Research Professor	Department of Botany Weber State University	2008-
Adjunct Professor	Department of Pharmacognosy, University of Illinois, Chicago	2006-
Adjunct Professor	Buck Institute for Aging, Marin	2006-2007
Adjunct Professor	Xishuangbanna Tropical Botanical Garden, China	2004-
Affiliate Professor	Ecology, Evolution and Conservation Biology Program, University of Hawaii	1999-2005

Environmental Awards

Rachel Carson Environmental Award	1999
Goldman Environmental Prize ($75,000)	1997
Nu Skin Force for Good Award ($10,000)	1996
American Freedom Festival Award	1993

All Publications

Books:

(7) Togashi T, Cox PA (editors). 2011. *The Evolution of Anisogamy: A Fundamental Phenomenon Underlying Sexual Selection*. Cambridge University Press, Cambridge, England.

(6) Cox PA. 2005. *Nafanua: Die Rettung des Samoanischen Regenwaldes* (translated by Suzanna Jamieson-Heinrichs) Dr. Gupta Verlag, Ratingen, Germany.

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Academic and Post-doctoral Experience

Senior Scientist	Brain Chemistry Labs / Institute for Ethnomedicine	2005-present
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Assoc. Professor of Biol.Sci.	California State University, Fullerton	2002-2007
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Publications (student co-authors in bold)

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Book

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JAMES SPENCER METCALF
Curriculum vitae

Degrees

Ph.D. (Microbiology)	University of Dundee, UK	1999
B.Sc. (2:i Honours, Marine Biology/Biochemistry)	Bangor University, UK	1995

Academic and Post-doctoral experience

Senior Researcher	Institute for Ethnomedicine	2013 – present
Adjunct Professor	Central Wyoming College	2014 - present
Associate member of staff	University of Dundee	2006 – 2016
Visiting Research Scholar	University of Mississippi	2008- 2012
Visiting Associate Professor	Weber State University, UT	2010- present
Post-Doctoral Research Fellow	University of Dundee	2000 – 2006

Publications

Peer-reviewed journals

(1) **Metcalf, J.S.,**, Banack, S.A., Wessel, R.A., Lester, M., Pim, J.G., Cassani, J.R., Cox, P.A. (2020). Toxin analysis of freshwater cyanobacterial and marine harmful algal blooms on the west coast of Florida and implications for eastuarine environments. *Neurotoxicity Research,* In press.

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