

Research on dopamine and Parkinson's disease illustrates value of exposome studies

By Annah Wyss

In a Feb. 5 seminar, "Reducing Neurotoxicity by Increasing Vesicular Capacity," hosted by the NIEHS Laboratory of Neurobiology, [Gary Miller, Ph.D.](http://cfusion.sph.emory.edu/Faculty/Profile.cfm?Network_ID=GWMILLE&DEPT=EOH), professor and associate dean for research at Emory University's Rollins School of Public Health, described his laboratory's NIEHS-funded research on dopamine and Parkinson's disease.

Specifically, Miller's group is studying how the alteration of the storage of dopamine, a neurotransmitter, may contribute to Parkinson's disease, a neurodegenerative disorder characterized by motor symptoms, such as tremors and slowed movement, and nonmotor symptoms, such as changes in cognitive abilities and mood. Disrupted storage of dopamine leads to the degeneration of dopamine neurons in the brain.

Pesticides, such as paraquat, and polychlorinated biphenyls (PCBs) have been linked to Parkinson's. Although many of these chemicals are now banned, they persist in the environment, causing continued human exposure. Since PCBs are known to inhibit storage of dopamine, characterizing the physiological effects of inhibited transport of dopamine may have important implications for understanding Parkinson's disease.

Regulation of dopamine linked with proteins VMAT2 and SV2C

Miller highlighted his lab's research on vesicular monoamine transporter 2 (VMAT2), a protein that helps regulate dopamine. Among mice with 90 percent reduced VMAT2 levels, Miller's group observed low levels of stored dopamine in vesicles. These mice were further characterized by overexpression of alpha-synuclein, a protein previously associated with Parkinson's disease, and exhibited symptoms similar to Parkinson's disease.

On the other end of the spectrum, mice with overexpressed VMAT2 appeared to be slightly more active and had vesicles that stored and released higher levels of dopamine, compared to wild-type mice.

Miller also described his research on synaptic vesicle glycoprotein 2C (SV2C), and the impact of the genetic deletion of SV2C. In discussing the motivation to study SV2C, Miller referenced other research on Parkinson's disease.

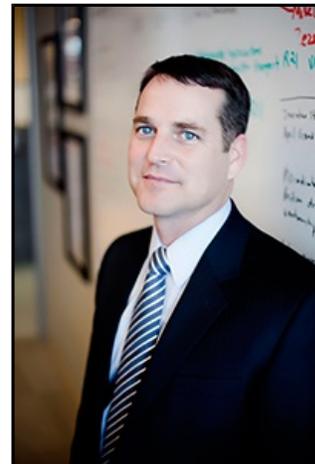
"Our interest in SV2C came from a genome-wide association study (GWAS) that integrated an environmental factor. Otherwise we wouldn't be looking at it," he explained.

Studying the exposome to advance public health

Miller also promotes the integration of environmental and genetic research as director of Emory University's Health and Exposome Research Center: Understanding Lifetime Exposures ([HERCULES](http://emoryhercules.com/)), an NIEHS Environmental Health Sciences Core Center. The center concentrates on studying the exposome, which Miller defines as the cumulative effect of environmental exposures on health over a lifetime.

"It is not just the exposures - it is how we respond to them," Miller reminded the audience. He said he hopes that efforts to understand the exposome will provide a set of tools to complement genomics analysis and provide a more comprehensive assessment of health outcomes, including the cause of Parkinson's disease.

(Annah Wyss, Ph.D., is an Intramural Research Training Award (IRTA) postdoctoral fellow with the Genetics, Environment, and Respiratory Disease Group.)



Miller's research demonstrates the effect of proteins VMAT2 and SV2C on vesicular storage of dopamine, offering insights into the relationship between pesticides and Parkinson's disease. (Photo courtesy of Gary Miller)

Environmental Factor in your publication, we ask that you provide us with a copy for our records. We welcome your [comments and suggestions](#).
(bruskec@niehs.nih.gov)

This page URL: NIEHS website: <http://www.niehs.nih.gov/>
Email the Web Manager at webmanager@niehs.nih.gov