

# Mice with frequent flier miles advance the Alzheimer's cause

January 4 2018

---



Olivier Thibault's lab at UK uses calcium imaging techniques to measure how neurons are affected over time. Thibault leads one of four groups in a multi-center grant to identify a biomarker for Alzheimer's disease. Credit: University of Kentucky Office of Public Relations and Marketing

Alzheimer's disease wreaks emotional havoc on patients, who are robbed

of their memories, their dignity, and their lives. It's financially devastating as well: care for Alzheimer's patients is predicted to top \$1 trillion by about the time children born today are having children of their own.

Alzheimer's begins its destruction decades before there are outward signs of memory loss, so some recent scientific effort has focused on recognizing the earliest signs that portend disease onset. Those telltale signs, called biomarkers, would enable patients to receive treatment for Alzheimer's sooner, thereby delaying the disease's devastating progress or stopping it altogether.

The biomarker treasure hunt has been difficult thus far. There's been little to no progress towards finding one that is a "triple threat:" noninvasive, inexpensive, and easily translatable to community populations. So, the National Institutes of Health called for research proposals to find new ways to diagnose Alzheimer's disease and predict its progression.

Among the grant applicants: a group of scientists from four different institutions, each with a specific scientific skillset that when put together had the resources to test the presence and reliability of one such biomarker.

"When I first saw the call for applications, I was really excited," said Dr. Olivier Thibault at the University of Kentucky's Department of Pharmacology and Nutritional Science. "I remembered some interesting work that came out of Dr. Bruce Berkowitz's lab at Wayne State University and thought it might be the cornerstone of a project that met the grant's parameters."

That cornerstone is called Quest MRI, a unique and dynamic process that is able to pinpoint levels of [oxidative stress](#) in specific regions of the

brain over time, and in living subjects. The technique is noninvasive and in most hospitals doesn't require expensive modifications to existing equipment.

"Almost everyone with a television set has heard about the benefits of antioxidant-rich vitamins like A, C, and E, and superfoods like blueberries, green tea, and dark chocolate," Thibault said.

"Well, antioxidants are the body's defense against something called free radicals. Free radicals are natural byproducts of chemical processes in the body, and in a healthy state [free radical production](#) is offset by the work of antioxidants. But when there are too many [free radicals](#), the balance is disrupted, and the resulting oxidative stress can increase risk for diseases like AD."

People write off the times when they can't remember where they left their keys, but realizing they don't know how to get home from the grocery store they've been visiting for years is a wake-up call that something is terribly wrong. The scientific term is "spatial disorientation," and it's a critical hallmark of Alzheimer's disease.

The capacity for spatial orientation lies in a part of the brain called the hippocampus. Berkowitz and Thibault hypothesized that using Quest MRI to measure oxidative stress in the hippocampus of a live animal and compare it to that animal's ability to remember how to navigate a maze could be proof of the existence of a biomarker for AD that met the NIH criteria of cheap, easy, and scalable. Even better: the process uses inexpensive drugs that are already FDA approved, making Quest MRI easily translatable to the general population.

The NIH was impressed, and awarded the foursome \$2.8 million over five years to test the hypothesis.

Rounding out the project are Dr. Geoffry Murphy at The University of Michigan and Dr. Brian Bennett at Queen's University (Canada). Bennett has developed a mouse genetically predisposed to high levels of oxidative stress, and Murphy's mice are already afflicted with Alzheimer's disease (AD).

Thus begins a roughly 850-mile circuit of testing where Bennett's oxidative stress mice are flown from Ontario to Ann Arbor, where Murphy puts them - and his own AD mice—through a maze to assess spatial navigation. Murphy himself then drives the mice to Detroit, where Berkowitz uses his Quest MRI to determine free radical production in the hippocampus. Ultimately, the mice end up in Thibault's lab, which uses calcium imaging techniques to measure how neurons are affected over time, thereby measuring the relationship between free radical production, oxidative stress, and behavioral changes in the same animal. Some of the mice actually make more than one circuit to assess cognitive and corresponding biochemical changes over time.

"The entire process provides a deeply characterized analysis of mice that may well affirm Quest MRI's ability to identify the earliest signs of Alzheimer's disease," Thibault said.

Even better, says Thibault, the group foresees a bonus aspect of their research: they will also be able to test the efficacy of pharmacologic and non-pharmacologic methods to reduce free radical production in the hippocampus. Advantageous data would point to the possibility of reducing free radical production using either an antioxidant "cocktail" or a light therapy called photobiomodulation.

Either option, said Thibault, would be "the cherry on the cake."

The project is in the early planning stages, and the mice don't begin their

journey until later this month, but Thibault and his colleagues are energized at the prospect of joining the hunt for a cure for Alzheimer's disease.

"To be able to identify or even predict Alzheimer's disease using Quest MRI, and then also be able to intervene using antioxidants or photobiomodulation, would be a one-two winning punch," Thibault said.

Provided by University of Kentucky

Citation: Mice with frequent flier miles advance the Alzheimer's cause (2018, January 4)  
retrieved 23 April 2024 from  
<https://medicalxpress.com/news/2018-01-mice-frequent-flier-miles-advance.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.