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2017 Part the Cloud: Translational Research Funding for Alzheimer's Disease (PTC)

### **Linking GSH and Cognitive Response: A Pilot Phase 2a Study of NAC in VCIND**

*Can a drug designed to boost levels of a key antioxidant in the brain help delay or prevent the onset of dementia?*

#### **Background**

Many neurological disorders, including Alzheimer's disease, involve problems with blood flow in the brain, which can cause oxidative stress and neurodegeneration. These vascular problems can occur at an early stage of brain disease, and they are linked to subtle declines in memory, task completion, and other cognitive functions. Scientists are looking for ways to treat people at this stage, known as vascular cognitive impairment with no dementia (VCIND), in order to prevent or slow the development of full-blown dementia. Such efforts, however, have been hindered because little is known about how blood flow loss and oxidative stress translates to cognitive decline. One clue is that studies have found that people with late-stage dementia have low levels of glutathione (GSH), a naturally produced compound that acts as an antioxidant. Thus, the loss of glutathione can make the brain more vulnerable to oxidative stress that will drive neuronal dysfunction and neurodegeneration.

#### **Research Plan**

Krista L. Lanctot, Ph.D., and colleagues will evaluate whether a compound known as N-acetylsysteine (NAC), which can boost glutathione production, may improve cognition and brain health in the study's participants. As part of this effort, the participants will receive a series of cognitive tests to determine how NAC treatment may improve cognitive function over time.

In addition, Dr. Lanctot and team will use newly-developed magnetic resonance spectroscopy (MRS) imaging techniques to evaluate the impact of NAC in study participants with VCIND and in those with healthy brains. These same individuals will receive beta-amyloid PET imaging to determine whether they have Alzheimer's-like brain changes as well.

#### **Impact**

Dr. Lanctot's study will evaluate whether NAC is a novel, safe drug therapy for moderating vascular brain problems and possibly delay or prevent dementia onset. In addition, this work could shed new light on how early-stage vascular problems in the brain may lead to dementia.

***Made possible through the generous funding from Part the Cloud, benefiting the Alzheimer's Association.***

#### **PI**

- Ph.D., Pharmacology, University of Toronto
- Senior Scientist, Sunnybrook Research Institute
- Executive Director of the Medical Outcomes and Research in Economics Research Centre
- Professor, Departments of Psychiatry, and Pharmacology and Toxicology, University of Toronto

#### **Research Category**

- Translational Research & Clinical Interventions

#### **Awards**

- Dr. Lanctot was an awardee of a New Investigator Research Grant from the Alzheimer's Association