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U of L neuroscientists awarded nearly \$2 million for research into Alzheimer's disease

Drs. Bruce McNaughton and Majid Mohajerani will investigate brain neurobiology related to Alzheimer's disease thanks to two grants worth nearly \$2 million over five years from the Canadian Institutes for Health Research (CIHR).

"We are extremely pleased about the success of the applications for these two research projects," says Dr. Erasmus Okine, vice-president (research) at the University of Lethbridge. "The number of people with Alzheimer's disease is expected to triple by 2050 and the costs of care will skyrocket. More than ever, we need to conduct research that will identify the mechanisms at work in Alzheimer's disease to allow for the development of effective treatments."

McNaughton, along with Mohajerani, Drs. Robert Sutherland and Boyer Winters (University of Guelph), received more than \$1.2 million to help determine the neural basis of cognitive reserve (CR), the main source of resilience against dementia and normal age-related cognitive decline. In humans, behavioural evidence indicates that CR is related to how much knowledge a person acquires over his or her lifespan. People who are bilingual and have a higher education status, school grades, occupational achievement and vocabulary show fewer symptoms of dementia. But the link between enhanced knowledge and CR needs to be experimentally established and the underlying neural mechanisms need to be determined.

In the mouse model, cognitive reserve is created by exposing mice to enriched environments where they can play, socialize and learn. The researchers will use state-of-the-art imaging technology to measure brain activity at rest and during encoding and retrieval of information, and the ways new and old memories interact in the brain. The measures will be correlated with measures of CR, age and the amount of amyloid deposits, or plaque, in the brain.

"We expect new and unanticipated insights into how the brain creates CR. This will help us establish a basis for comparison with abnormal brain dynamics that may be associated with normal aging and age-related dementia," says Sutherland. "We're taking this project forward in other awards in the direction of applying the same neuroscience information to aging humans in collaboration with the University of California Irvine and the U of L."

In the other project, Mohajerani, along with Dr. Robert McDonald and McNaughton, received nearly \$700,000 to probe the link between amyloid deposits in the brain and functional alterations of specific brain networks.

Amyloid deposits, made up of amyloid beta peptide, are plaques that form between brain cells and are a feature of Alzheimer's disease, as is the presence of tangles, made up of tau proteins that form inside brain cells.

"Using a second generation of a mouse model of Alzheimer's disease, we intend to determine how early and in what part of the brain the amyloid beta plaques form," says Mohajerani. "We don't know in full detail the temporal dynamics and spatial distribution of amyloid plaque formations and how they contribute to neuronal activity and network dysfunction and behavioural and cognitive impairment in Alzheimer's disease."

The first symptoms of Alzheimer's disease in humans are spatial navigation deficits and disorientation. Mohajerani wants to focus on brain neurons that serve as the brain's compass or navigation system and examine how the formation of amyloid plaques affects those neurons. Preliminary data shows that neurons located next to plaques become either hyperactive or hypoactive. Previous research using functional MRI studies have shown that brain network activity in humans becomes altered 25 years before any cognitive symptoms, such as memory loss, are evident.

"We are very privileged to become one of the centres in Canada to investigate how formation of amyloid beta plaques leads to brain cell death and subsequently to dementia," says Mohajerani. "An Alzheimer's crisis is bearing down on us like a tsunami and this is something we need to take seriously. Within 10 years, Alzheimer's is going to be the costliest disease in Canada and perhaps everywhere in western countries."

Seed funding for both projects came from Alberta Innovates, the Alberta Prion Research Institute and the Alzheimer Society of Alberta & Northwest Territories.

"If we didn't have this seed funding, we wouldn't have gotten to this point," Mohajerani says.

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Contact:

Caroline Zentner, public affairs advisor

403-394-3975 or 403-795-5403 (cell)

caroline.zentner@uleth.ca