New research yields insights into Parkinson's disease

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Researchers at the University of Toronto Scarborough (UTSC) used an innovative technique to examine chemical interactions that are implicated in Parkinson's Disease.

The work details how a protein called alpha-synuclein interacting with the brain chemical dopamine can lead to protein misfolding and neuronal death.

Parkinson's Disease is a neurodegenerative disease which results in loss of motor control and cognitive function. Although the cause isn't known precisely, the disease involves the death of brain cells that produce dopamine, a chemical important in neuronal signaling. The disease also involves a protein called alpha-synuclein which aggregates in the neurons of people with the disease.

Kagan Kerman, a chemist in the Department of Physical and Environmental Sciences, and Ian R. Brown, a neuroscientist who founded UTSC's Centre for the Neurobiology of Stress in the Department of Biological Sciences, looked at the way dopamine interacts with alpha-synuclein to form aggregates that may be toxic to neurons.

"This is very fundamental," says Kagan Kerman. "It gives us a new point of view of the misfolding proteins and how they are affected by dopamine."

These sorts of interactions are often studied using microscopy. But the UTSC researchers decided to use an electroanalytic technique called voltammetry. By studying tiny changes in electric current as dopamine and alpha-synuclein interacted they were able to determine details about the early phases of the interaction.

Using the technique, they were able to detail how changes in pH levels and ionic strength of the solution affected the interaction. They found that at higher pH levels and higher ionic strengths, dopamine interacted much more strongly with alpha-synuclein, forming aggregates more quickly.

The results could have implications for understanding and treating the disease. Normally dopamine is contained in structures called vesicles, in which pH levels are low and dopamine is unlikely to interact with alpha-synuclein. Outside of the vesicles dopamine encounters higher pH levels and, according to the new research, is much more likely to interact to create aggregates.

The analysis was done using chemicals deposited onto screen-printed electrodes only 12.5 mm by 4 mm. The electrodes were manufactured at Osaka University, where Kerman completed his PhD work. Because they are so small, the electrodes allowed analysis to be done on tiny samples.

The technique is a potentially quicker and cheaper way to study protein misfolding, and could be automated to screen drugs that might treat the disease, says Brown.

The research was published in *Chemical Neuroscience*, published by the American Chemical Society.

Provided by University of Toronto Scarborough