MedicalXpress

Role of amyloid beta as sensors and protectors in Alzheimer's and other diseases explored

March 27 2012

Alzheimer's disease is the sixth leading cause of death in the United States and the only cause of death among the top 10 in America without a way to prevent, cure or even slow its progression, according to the Alzheimer's Association. Today, 5.4 million Americans are living with the disease, and another American develops it every 69 seconds.

Unfortunately, many Alzheimer's disease drugs targeting the misfolding of the amyloid beta protein have failed clinical trials, leading some to question the validity of the amyloid hypothesis.

In upcoming issues of the *Journal of Alzheimer's Disease*, Dr. Ian Murray of the Texas A&M Health Science Center College of Medicine provides a new way of looking at amyloid – not only in Alzheimer's, but also in other amyloid diseases – with a hypotheses paper and separate supporting data paper.

Murray, Ph.D., assistant professor in the Department of Neuroscience and Experimental Therapeutics in the college, is one of four authors on a hypotheses paper supporting Amyloids as Sensors and Protectors (ASAP). This hypothesis incorporates both the emerging idea that amyloid is protective and the pathological amyloid hypothesis.

Amyloid senses cellular environmental stress, such as elevation of reactive metabolites and oxidative products or metals, and then misfolds.

This misfolding initiates a protective cellular response in the short term. Long-term or chronic stress such as metabolic dysfunction (diabetes) would lead to the pathological consequences of amyloid misfolding (as diabetes is a risk factor for Alzheimer's).

This interesting ASAP hypothesis is supported by existing publications in the Alzheimer's disease field, as well as from several other amyloid diseases. It also explains several disparate findings in the field and suggests further experiments to test the hypothesis.

In the supporting data paper, Dr. Murray and four other authors mechanistically linked diabetes and Alzheimer's. They demonstrated the first part of the ASAP hypothesis – amyloid can detect metabolic dysfunction. Reactive metabolites, elevated during metabolic dysfunction such as diabetes, chemically modify and misfold the amyloid protein in the test tube. These metabolites play a role in chemical glycation reactions to eventually form advanced glycation end products.

Dr. Murray demonstrates, similar to previous reports, that such modifications localize to the misfolded amyloid in Alzheimer's disease.

Provided by IOS Press