Increased dementia risk in women – a matter of proteins?

Gender-specific differences between the levels and structures of proteins present in the white matter and the mitochondria of the brains of men and women suffering from dementia have been revealed for the first time in a study published in the open access journal *Molecular Brain*.  
  
While previous studies have shown that women exhibit higher risk of dementia than men, the underlying mechanisms of this gender difference have remained elusive. The findings by researchers from Nanyang Technological University, Singapore may advance our understanding of the higher risk of dementia that has been observed in women compared to men, which the researchers suggest could lead to the development of new drugs for dementia treatment.

Associate Professor Sze Siu Kwan one of the co-authors of the study said: “The number of dementia patients is projected to triple by 2050 and there is an urgent need to identify key mechanisms of how dementia develops. Our findings and further study could have direct implications for our knowledge about the progression of dementia that could lead to the development of drugs for treatment of dementia.”

The researchers used proteomics – the large-scale study of proteins, including their variations and changes – to analyze the proteins present in post-mortem brain tissues from five male and five female dementia patients and ten healthy controls. The researchers wanted to identify changes in structure and function of the proteins present in the white matter and the mitochondria of the temporal lobe – the part of the brain involved in visual memory and the understanding of language. Proteomics is an unbiased approach as, rather than testing a set of pre-defined, specific proteins, it allowed the researchers to look at thousands of proteins to identify changes associated with dementia.

Degenerative Protein Modifications (DPMs) are changes to proteins that are thought to cause the loss of protein function, similar to the way that steel loses strength when rusting. The protein shown to be most affected by these DPMs in the brains of dementia patients in this study is Myelin Basic Protein (MBP) which is important for the production of a protective myelin layer around the axons of nerve cells. Axons are part of the brain’s white matter which transmits signals between different parts of the brain. A process called myelation provides an electrically insulating layer around axons, similar to the insulation around an electrical wire. Damage to that insulating layer can stop electrical impulses from being conducted properly, disrupting communication between different parts of the brain. DPMs that are thought to increase the dysfunction of MBP were found to be more pronounced in women than in men. Sze Siu Kwan said: “As DPMs are likely to critically influence protein function and activity in the central nervous system they can be novel drug targets for treatment of dementia.”

The researchers detected changes in the presence of certain proteins in the mitochondria of patients suffering from dementia that indicate mitochondrial dysfunction. Mitochondria are responsible for creating energy needed to sustain proper cell function, including brain cell function. Mitochondrial dysfunction can lead to cell injury or even cell death. As with changes to other proteins, disturbance to the proteins in the mitochondria was observed to be more pronounced in women than in men.  
  
Xavier Gallart-Palau, the first author of the paper said: “The findings of this study indicate that proteomics can detect differences between male and female dementia patients on a molecular level which cannot be detected by standard approaches.”  
  
The findings also provide new insight into the molecular basis of increased risk and severity in women suffering from dementia. They may be a step towards future clinical interventions targeted at reducing dementia risk in both men and women.  
  
**-ENDS-**

Media Contact  
Anne Korn  
Press Officer  
BioMed Central  
T: +44 (0)20 3192 2744  
E: anne.korn@biomedcentral.com

Notes to editor:  
1. Gender differences in white matter pathology and mitochondrial dysfunction in Alzheimer’s disease with cerebrovascular disease  
Xavier Gallart-Palau, Benjamin S. T. Lee, Sunil S. Adav, Jingru Qian, Aida Serra, Jung Eun Park, Mitchell K. P. Lai, Christopher P. Chen, Raj N. Kalaria and Siu Kwan Sze  
Molecular Brain 2016  
DOI: 10.1186/s13041-016-0205-7

The article is available at the [journal website](http://molecularbrain.biomedcentral.com/articles/10.1186/s13041-016-0205-7).   
  
Please name the journal in any story you write. If you are writing for the web, please link to the article. All articles are available free of charge, according to BioMed Central's open access policy.  
  
2. *Molecular Brain* is an open access, peer-reviewed journal that considers manuscripts on all aspects of studies on the nervous system at the molecular, cellular, and systems level providing a forum for scientists to communicate their findings.

Molecular brain research is a rapidly expanding research field in which integrative approaches at the genetic, molecular, cellular and synaptic levels yield key information about the physiological and pathological brain. These studies involve the use of modern techniques such as approaches of molecular biology, genomics, proteomics, modern electrophysiology and neurobiology.  
  
3. BioMed Central is an STM (Science, Technology and Medicine) publisher which has pioneered the open access publishing model. All peer-reviewed research articles published by BioMed Central are made immediately and freely accessible online, and are licensed to allow redistribution and reuse. BioMed Central is part of Springer Nature, a major new force in scientific, scholarly, professional and educational publishing, created in May 2015 through the combination of Nature Publishing Group, Palgrave Macmillan, Macmillan Education and Springer Science+Business Media.