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PRESS RELEASE
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HOW GENES AND HEALTHY LIFESTYLE HELP PROTECT AGAINST BRAIN DEGENERATION

The interaction between genes and lifestyle is a crucial factor in diseases such as Alzheimer's and Huntington's. Neuroscientists from Scotland and Australia today (Wednesday 15 July) described how exercise and a healthy diet can help protect against neurodegeneration in later life, whereas stress and inflammation can damage brain cells. These findings could also point the way to new treatments.

Professor Anthony Hannan at the Florey Institute, University of Melbourne conducts research on mouse models of Huntington's disease, including their gut microbiota – that is, harmless micro-organisms that live in the saliva and gut and are essential for many biological functions. His group has discovered that changes in gut microbiota are associated with the early stage of Huntington's disease. The so-called gut-brain axis suggests that an unhealthy gut can be associated with an unhealthy brain.

"We don't know whether the altered microbiota contribute to the cognitive changes, psychiatric symptoms and movement disorders seen in Huntington's and other neurodegenerative diseases. That is the next big question," said Professor Hannan, speaking at the FENS Virtual Forum of Neuroscience.

For many years, Professor Hannan has been investigating genetic and environmental risk factors and how a person's predisposition to particular brain disorders might be influenced by stress, exercise and cognitive stimulation. This is referred to in science as 'gene-environment interaction'. Studies in mice in his lab have shown that regular exercise and cognitive stimulation can slow the onset and delay progression of Huntington's disease.

Other studies on the negative effects of stress are also linked to exacerbating neurodegenerative disease. Exposure to stress can directly affect the composition of the microbiota and alter the balance of the natural bacteria in the gut. Whilst genetic factors can cause both gut and brain dysfunction, environmental factors such as stress, exercise and diet may modulate brain function via the gut, and therefore we must better understand this complex, dynamic interaction between the brain and the body.

"Putting all this together, the gut can communicate with the brain through neurons, hormones and the immune system to modify brain function, behaviour and, more remarkably, cognition," said Professor Hannan. This new knowledge, and other studies of the therapeutic effects of healthy lifestyle, is contributing to an emerging treatment strategy that Professor Hannan has proposed, known as enviromimetics, novel drugs that mimic or enhance the beneficial effects of physical activity, cognitive stimulation and other lifestyle factors.

"Huntington's disease is an example of a disease where animal models translate well to human conditions. Because of the overlapping mechanisms mediating different brain diseases, we hope these findings can be used more widely for other disorders such as Alzheimer's disease, other kinds of dementia, and depression," he said.

Chronic inflammation is known to have an important role in neurodegenerative disease and dementia. **PhD student Anna Stevenson from the University of Edinburgh** is trying to determine why it is harmful, and how it relates to cognitive ability. "As we age, there is a shift in the inflammatory state whereby it keeps going beyond the point of doing good and instead starts to damage brain cells," she said.

To find the answer, Ms Stevenson is focusing on an epigenetic mechanism called DNA methylation. Epigenetics is the study of changes to the function of our genes but not the DNA itself. "If we think of our DNA sequence like a book, epigenetics can be thought of as the punctuation: changing the way this book is read without altering the sequence of letters," she explained. DNA methylation is the changing patterns of DNA activity throughout life.

In this study, she looked for signs of inflammation in blood and in post-mortem brain tissue of 14 people aged between 70 and 79, none of whom had a diagnosis of neurodegenerative disease before they died to explore its relationship with ageing and cognitive ability.

Her results suggest that the changing patterns of DNA activity associated with inflammation might be detrimental to cognitive functioning. With more research, she hopes that the research team might be able to use these patterns to better understand the role of inflammation in cognitive ageing and Alzheimer's disease.

Commenting on the research presented at FENS, **Professor Tara Spires-Jones from the University of Edinburgh** (chair of the symposium) said that this is an exciting time in understanding diseases of the ageing brain. "We now know that we can modify our risk of many brain diseases associated with ageing by making changes to our daily lives. While some people are unlucky and are likely to develop dementia based on the genes they inherit, current data suggest that as many as one third of dementia cases could be prevented by modifying our lifestyles. We can harness the brain's resilience by increasing exercise, eating a healthy diet, and not smoking to protect the brain from disease like Alzheimer's.

"This symposium highlights that understanding the biology of a disease and how to treat it requires a range of research approaches including animals, humans and technology," she concluded.

END

Symposia 56: Gene-environment interactions modulating brain ageing, neurodegeneration and dementia
Abstracts: *Anthony Hannan* **-** Gene-environment interactions and experience-dependent plasticity as modulators of neurodegenerative disease
Anna Stevenson - Influence of inflammation and epigenetics on cognitive abilities in ageing

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NOTES TO EDITORS

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Anna Stevenson, PhD student, Tara Spires-Jones research group, University of Edinburgh, UK

Tara Spires-Jones, Professor, Centre for Discovery Brain Sciences, https://www.ed.ac.uk/discovery-brain-sciences/our-staff/research-groups/prof-tara-spires-jones

Further Reading (Hannan)

Microbiome profiling reveals gut dysbiosis in a transgenic mouse model of Huntington's disease. Kong, Lê Cao, Judd, Li, Renoir, Hannan. *Neurobiology of Disease* 2018, **DOI: 10.1016/j.nbd.2018.09.001**

Exercise, diet and stress as modulators of gut microbiota: Implications for neurodegenerative diseases. Gubert, Kong, Renoir, Hannan. *Neurobiology of Disease* 2020, **DOI: 10.1016/j.nbd.2019.104621**

Transgenic Mouse Models as Tools for Understanding How Increased Cognitive and Physical Stimulation Can Improve Cognition in Alzheimer's Disease. Shepherd, Zhang, Zeleznikow-Johnston, Hannan, Burrows. *Brain Plasticity* 2018, 4; 127-150, **DOI: 10.3233/BPL-180076**

The 12th FENS Virtual Forum of Neuroscience
As a consequence of the COVID-19 pandemic, the FENS Forum 2020 will be held entirely virtually.

The FENS Forum of Neuroscience is the largest basic neuroscience meeting in Europe, organised by the Federation of European Neuroscience Societies and hosted by the British Neuroscience Association. It will attract around 5,000 international delegates. FENS was founded in 1998. With 44 neuroscience member societies across 33 European countries, FENS as an organisation represents 20,000 European neuroscientists with a mission to advance European neuroscience education and research.