Linking Alzheimer’s and nutrition

As head of her lab, Assistant Professor Ai-Ling Lin speaks about her team’s work to develop dietary and pharmacological interventions to slow down brain ageing and the progression of Alzheimer’s disease.

How have your experiences travelling the world as a child with missionary parents to visit people in churches and hospitals, as well as inspiration by the likes of Isaac Newton and Albert Einstein, influenced your work?

I wanted to be a physicist, but also hoped to be able to help and care for people in some way. Having a PhD in medical physics and working in the medical research field made both of these dreams come true. On the one hand, I acquired in-depth knowledge of physics and engineering of medical imaging, while on the other, I applied the technology to address important medical issues through basic research and clinical investigations. Now, using magnetic resonance imaging (MRI), my research goal is to develop surrogate markers that might detect brain function changes in ageing and Alzheimer’s disease at an early stage. Ultimately, this could lead to the identification of effective therapeutics to slow down brain ageing and prevent Alzheimer’s disease.

Your mouse model study shows that caloric restriction is associated with preserved vascular function. Can you provide further insight into the nutritional intervention arm of your research?

Brain vascular integrity plays a major role in determining cognitive functions, such as learning and memory. In our studies, we found that old mice treated with caloric restriction had preserved cognitive functions when compared with young mice. Our findings are also consistent with others, showing that caloric restriction impedes cognitive impairments in mouse models of human Alzheimer’s disease. In addition, caloric restriction improves insulin sensitivity and preserves glucose homeostasis, which contrasts diabetes. Through our research findings, we suggest that nutritional interventions are crucial and effective to preserving cognition in ageing and reducing risks for Alzheimer’s disease.

The other arm involves the use of rapamycin. Your research found that mice treated with the therapeutic agent had restored cerebral blood flow, blood-brain barrier integrity and glucose metabolism compared to age- and gender-matched wild-type controls. How effective could this be for humans?

Rapamycin is a drug approved by the US Food and Drug Administration. It has been widely used in the clinic and was originally used as an immunosuppressive agent to prevent the rejection of organs in transplant patients. It is now also being used as an anti-tumour agent. We learned from recent studies that rapamycin can improve immune functions in the elderly with minimal side effects when the dosage is carefully implemented. All of this indicates that rapamycin can be safely used in humans and have multiple beneficial effects. However, it has not been applied to age-related neurodegenerative disorders, nor has neuroimaging been applied to study the treatment efficacy of rapamycin on neurovascular and neurometabolic functions in humans. It is our future goal to bring rapamycin to clinical trial for this purpose.

What role should governments play in the service and education of their citizens regarding healthy diets?

I think governments can have at least three major functions. First, they can develop programmes to ensure access to healthy, high-quality food. For example, the New York City Department of Health developed an innovative programme incorporating street vendors, and the Mayor of Philadelphia helped build a supermarket to help people in the neighbourhood get access to fresh fruit and vegetables. Second, governments can also develop programmes to educate their citizens on how to choose healthy diets. For instance, I have seen ‘traffic light’ programmes to indicate the foods you can consume always (green), sometimes (amber) and less often (red). Finally, governments (state and federal) can ensure funding and financial support for research and education to address health disparities.

Can you describe your future research goals?

Unlike the ‘one-size-fits-all’ approach, precision interventions take into account individual differences in people’s genes, gut microbiome, environments and lifestyles. In the 2015 State of Union address, President Obama indicated that precision medicine will be a “bold new research effort to revolutionise how we improve health and treat disease”. For nutrition, researchers have developed algorithms to prescribe personalised diets by lowering post-meal blood sugar responses. This can also apply to the prevention of dementia. In the future, we would like to be able to provide personalised medicine advice for patients with brain disorders and monitor their progress using neuroimaging and cognitive testing.
The human brain is the main organ of the central nervous system; it receives input from all sensory organs and communicates with all muscles to enable their movement. Of all the vertebrates, the human brain is the largest relative to body size. Although the brain represents only about 2 per cent of a person’s total body weight, it utilises 20 per cent of oxygen and 25 per cent of glucose in the human body. While this energy supply is normally obtained from blood glucose, the brain is able to source alternative energy from ketone bodies during periods of low glucose, such as when fasting or exercising, or due to limited carbohydrate intake.

It is generally considered that healthy functioning of the brain relies upon the maintenance of cerebral metabolic rates of glucose and blood flow. A decrease in these rates, as happens with ageing, leads to functional losses resulting in a wide range of neurodegenerative conditions – one of which is Alzheimer’s disease, the sixth leading cause of death in the US.

It is known that age is one of the biggest risk factors associated with the onset of Alzheimer’s. Thus, as members of the ever-burgeoning global population continue to live longer, the need to understand the precise disease mechanisms becomes increasingly pressing. This would enable the development of more effective intervention strategies and therapeutics, relieving the burden of Alzheimer’s for individuals and wider society.

Type 2 diabetes and Alzheimer’s

With that in mind, a researcher based at the University of Kentucky has been conducting a wide variety of investigations to better understand brain ageing and the progression of Alzheimer’s disease. Assistant Professor Ai-Ling Lin heads the Lin Brain Laboratory, where research into preserving brain functions for individuals at high risk of Alzheimer’s disease is performed.

In addition to age, it is known that type 2 diabetes also dramatically increases the risk of developing Alzheimer’s. “Impaired glucose utilisation, abnormal blood glucose levels and dysfunctional insulin signalling – known as insulin resistance – are the major symptoms of individuals with type 2 diabetes,” explains Lin. “More and more evidence shows that patients with Alzheimer’s disease have insulin resistance in the brain, which impairs the energy supply to neurons and leads to cognitive defects.”

The weight of evidence supporting this resistance to insulin is shown in the increased recognition of Alzheimer’s disease as ‘type 3 diabetes’.

Restricting caloric consumption

One investigation Lin has led is to better understand how restricting caloric intake can increase ketone body metabolism and preserve...
And, although the relationship is extremely complicated and not fully understood, there is a wealth of evidence suggesting a link between poverty and obesity.

One reason for this association is that individuals in impoverished regions have poor access to fresh food, but there is also evidence supporting the idea that people living in poor countries are less active. There are several reasons for this, including the fact that violence tends to correlate with poverty, so individuals become more reluctant to venture outside through fear. In addition, poor people are less likely to be able to afford things such as exercise equipment and gym memberships.

Lin is therefore intent on encouraging governments to provide services and education for their citizens regarding the importance of healthy diets. “Governments can play a crucial role in facilitating the supply of quality food to these areas,” explains Lin. “I believe that with the support of governments, people could obtain higher quality nutrition and make better decisions regarding their diet.” Crucially, Lin emphasises the need to educate children.

If the importance of a balanced diet can be instilled in an individual at a young age, it is far more likely to stay with them throughout their lives. And, significantly, this information would be cascaded down to their children, thereby becoming common practice for all society. Another goal for Lin is to encourage governments to provide funding and financial support for research and education to solve health disparities.

Much has been made of the increasing prevalence of type 2 diabetes on a global scale and the need to eat healthily. However, with Lin’s research activities, the onset of neurological diseases such as Alzheimer’s – or type 3 diabetes – can be prevented. Ultimately, these findings help inform government programmes that can facilitate a healthy mind and body.