THE UNIVERSITY OF QUEENSLAND AUSTRALIA

RESEARCH IMPACT

DISCOVER — ENGAGE — IMPACT

MEMORY MAKERS

Building on forty years of existing research, UQ neuroscientists are now conducting clinical trials to prove that exercise can prevent and reverse cognitive decline, such as dementia.

With the average human lifespan expected to hit 100 years in the not-too-distant future, for many people, the idea of living with cognitive decline evokes a greater fear than death.

"Ultimately, our brain is who we are," says Professor Perry Bartlett, founding director of the Queensland Brain Institute (QBI) and Foundation Professor of Molecular Neuroscience.

"As we age, our brain experiences what is called 'cognitive decline' – a loss in abilities related to memory, language, learning and spatial navigation. We fear losing who we are."

But what if cognitive decline was not inevitable? What if it could be reversed?

QBI's Professor Bartlett, Dr Daniel Blackmore and Dr Mia Schaumberg are working to answer these questions. In collaboration with the School of Human Movement and Nutrition Sciences and the Centre for Advanced Imaging, they are currently recruiting volunteers to understand whether exercise can increase the production of new brain cells and improve learning and memory in the ageing brain.

The biggest health crisis of our time

Currently, three of the top five diseases globally that cause early death or an inability to work are diseases of the brain: dementia, stroke and depression. A report released by Alzheimer's Australia in 2016 states that dementia is one of the major chronic diseases of this century. The health, social and economic costs to society are enormous; the emotional burden on families can't be valued.

Working to prevent or reverse these diseases is essential. A 2007 study states that by 2050, the number of people living with dementia will quadruple – 1 in 85 people worldwide. The study estimates that if interventions could delay the onset of the disease and its progression by just one year, there would be 9.2 million fewer cases of Alzheimer's disease in 2050.

The impact of any successful intervention on the health burden could be staggering.

But first we need to understand how the brain functions.

Understanding brain function

Professor Bartlett's work is focused on understanding how the brain produces new neurons. This process, neurogenesis, is now accepted to be a process that occurs normally in the healthy adult brain, thanks to a discovery Professor Bartlett made in the 1990s. He led a team of researchers who discovered stem cells in the hippocampus, a region of the brain responsible for learning, spatial navigation and encoding new memories. The discovery challenged the belief that the number of neurons we're born with is fixed and that the brain was unable to regenerate.

In 2017, Professor Bartlett and other QBI researchers made the world-first discovery that new adult brain cells are also produced in the amygdala, a region of the brain important for processing fear and emotional memories.

As the brain ages, our ability to learn and remember generally declines. These changes are thought to occur as a result of decreased neurogenesis, resulting in impaired cognitive function and mood regulation.

New neurons appear to have two main properties: they respond to and encode incoming information better than older neurons, and they seem to be able to control the overall level of activity in the hippocampus. While constantly updating the level of activity in the hippocampus is better for learning and memory storage, the problem is – unlike the hippocampus in young people, which can recover from neuron loss spontaneously – the older hippocampus appears to have run out of steam. It also shrinks quite considerably in aged patients showing cognitive decline.

However, Professor Bartlett's team has discovered that stem cells in the hippocampus, the 'precursor' cells that create new neurons, are not lost in the ageing brain, but are just dormant. Postdoctoral Research Fellow Dr Daniel Blackmore has shown that, at least in mice, these stem cells can be activated by exercise.

"While exercise can increase the production of new brain cells and improve learning and memory, it's much more complicated than that," Dr Blackmore says.

"It appears that waking dormant stem cells in the brain requires quite precise periods of exercise – too much or too little does not have the same impact. You need to hit a 'sweet spot'. We want to know if this could be true for humans too."

Hitting the 'sweet spot'

Postdoctoral Research Fellow in Exercise and Dementia Dr Mia Schaumberg, who describes herself as a 'research translator', is using Professor Bartlett and Dr Blackmore's findings to inform a clinical trial investigating the effect of different exercise intensities on the ageing brain.

"It gets pretty busy in here," says Dr Schaumberg as she walks through the recently established UQ Centre for Exercise and Healthy Brain Ageing.

"We currently have 120 healthy volunteers aged 65–85 who have signed up to be closely monitored as they exercise at UQ three times a week for six months, but we are looking for a total of 300."

Participants are divided into three groups according to the level of exercise they undertake: light intensity, moderate intensity or aerobic intervals. All exercise is supervised and monitored. The trial will measure volunteers' cognitive function, fitness, blood hormones, genetic factors and brain volume before beginning exercise, at regular intervals during the exercise program, and six months after the end of the program.

"We'll also be measuring changes in the volume of participant's brains, and in the brain's connectivity – how regions of the brain communicate with one another," she says.

Understanding how exercise affects the brain

While Dr Schaumberg has personal motives for conducting this research – with a close family member suffering from cognitive decline and memory loss – she believes the study itself is already benefiting the volunteers.

We have hosted Centre morning teas to foster social connections between participants, students and staff, and one of our students even does gardening for a participant!

We hope that people maintain these connections and continue to exercise together after their participation in the trial is over.

"Creating a sense of community makes people more motivated to stay involved in this type of research."

And this continuity of involvement is important for the research.

"The problem is that we don't have the research to say definitively what is the best exercise for the brain and why is it the best.

While small lifestyle changes can be beneficial to brain health, our research aims to find out what is optimal – what will make a practical difference to people's lives," Dr Schaumberg says.

A long road

Professor Bartlett agrees.

"When I began exploring the brain in 1977, the prevailing idea was that the adult brain was static and unchangeable – which didn't make sense to me," he says.

"If our research works, we should have a way of working out what the correct exercise is for stimulating the production of nerve cells, we will see a drastic reduction in cognitive decline in a population of ageing people, and we will see the development of some of these molecules that we know regulate the exercise phenomena into a pharmaceutical reagent for people for whom exercise is perhaps not appropriate or not enough.

"Ultimately, we hope to have clear public health guidelines as to how exercise can both prevent and reverse dementia."

"If we can change the cognitive outcomes for these people over the next decade or so, then we can change the lives of people with dementia and defray the economic cost – both to people and to society."

The next steps – can you help?

The clinical trial is a collaboration between UQ's Queensland Brain Institute, the UQ School of Human Movement and Nutrition Sciences and the UQ Centre for Advanced Imaging and is funded by a $2.1 million donation from the Stafford Fox Medical Research Foundation.

Would you like to join the exercise study?

Healthy men and women aged 65–85 are invited to participate in a six-month supervised exercise program. To be eligible, participants must have no history of stroke or brain trauma, no diagnosed mental illness or cognitive function impairment, be free of significant cardiovascular disease, have a healthy BMI (< 30 kg/m2), and be able and willing to commit to the duration of the exercise program. Participation will include fitness tests, cognitive function testing, MRI scans of the brain, and small blood samples.

To register for the clinical trial, contact Dr Mia Schaumberg and the Healthy Brain Ageing Team on 07 3346 8770 or healthybrains@uq.edu.au or visit the exercise web page.

uq.edu.au/research/impact

(Image credit: Getty/ 851958262)

The long road:

1982: Professor Bartlett predicts the existence of stem cells in the brain

1992: Professor Bartlett is the first to demonstrate conclusively the existence of stem cells in the embryonic forebrain of adult mice, a seminal discovery providing definitive evidence for the concept of brain stem cells and the production of new nerve cells in the adult human brain

2001: Professor Bartlett's group identify and isolate a stem cell in the brain for the first time

2010: Professor Bartlett's group demonstrate that there are large numbers of quiescent stem cells that can be activated to produce new neurons, even in the older brain

2012: Dr Daniel Blackmore shows that stem cells in aged mice can be activated by exercise

2016: Led by Professor Bartlett, the UQ Centre for Exercise and Healthy Brain Ageing is established

2017: Clinical trial for testing the impact of exercise on the human brain begins

Contact details:

The UQ Centre for Exercise and Healthy Brain Ageing
Email: healthybrains@uq.edu.au
Phone: +61 7 3443 3209
Web: UQ Researchers
Twitter: @QldBrainInst

To register for the clinical trial:
Email: healthybrains@uq.edu.au
Phone: 07 3346 8770
Web: qbi.uq.edu.au/study-exercise-and-cognition-older-adults