Alzheimer's disease linked to heart's effect on the brain

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The prevailing medical wisdom that Alzheimer's Disease has its origins in the brain has a radical and disputed rival with shocking implications for medicine's relentless efforts to forestall disease, ageing and death, according to a new review of the evidence.

If the rival theory is correct, it will require a major rethink of drug therapies, and the level and direction of research investments, currently aimed at preventing and treating a disease that will soon engulf 100 million globally.

Alzheimer's is the most common form of dementia, and involves loss of memory and other intellectual abilities serious enough to interfere with daily life. Also known as age-related dementia, it accounts for 60 to 80 per cent of all dementia cases.

The established medical view is that Alzheimer's is primarily a degenerative disease of the brain caused by the effects of accumulating protein deposits - known as "beta-amyloid" senile plaques and "neurofibrillary tangles" - that interfere with neural pathways and signaling.

Whether these plaques and tangles are the primary cause for the onset of Alzheimer's is still uncertain. Some people develop plaques in brain tissue as they age without developing Alzheimer's, and it's still unknown whether plaques cause the disease or whether they're a by-product of the Alzheimer's disease process.

But the alternative explanation argues that aged-related dementia has an earlier origin in the heart and vascular system, not the brain.

"Aged-related dementia is the result of undetected bleeding into the brain caused by the lifelong destructive effects of the heart's pulse on tiny blood vessels in the brain," says Jonathan Stone, Professor of Neurobiology at the University of Sydney.

Together with colleagues from the University of Sydney and the Victor Chang Cardiac Research Institute, Stone led a recently published comprehensive review assessing the vascular explanation for age-dementia in the *Journal of Alzheimer's Disease*.

"If we live to old age, the heart destroys us. That's the conclusion more scientist are beginning to take seriously," he says.

"We propose that dementia is primarily vascular, caused by the destructive effect of the pulse on the cerebral blood vessels, with the loss of neurons and the pathology that Alois Alzheimer described over a century ago occurring secondarily to vascular breakdown.

"We argue, further, that dementia is age-related because the pulse becomes more intense and destructive with age."

Over the course of a lifetime, the aorta gradually hardens as the elastin in the wall of the aorta starts to fail. As an analogy, a 20 year-old's artery is like a flexible balloon, while an 80 year-old artery is more like a stiff hard garden hose.

"As this hardening happens, the aorta causes higher peaks and troughs resulting in higher blood pressure as a person ages," says Stone. "With blood spurting into them with increasing intensity, the brain's blood vessels become damaged.

A major contribution to understanding has come from the insights of research cardiologists, in particular Dr Michael O'Rourke of the Victor Chang Institute, who has drawn a correlation between age-related stiffening of the aorta and an increase in the intensity of the pulse. This may be the factor which links age to dementia.

This is a radical idea, likely to attract its share of controversy, but one supported by several other lines of evidence.

Doctors were already reconsidering the role of blood vessels in dementia more than a decade ago when major international studies revealed, unexpectedly, that people on blood pressure medication were at lower risk of dementia.

Today, medical experts agree that dementia and cardiovascular disease - diseases of the heart and blood vessels, including stroke - share a set of well defined risk factors: high blood pressure, high levels of low-density lipoprotein (LDL) cholesterol, smoking and obesity.

What's to be done?

The vascular explanation provides a rationale for prevention - anything in diet or exercise or weight control that protects our cardiovascular system is already known to protect against dementia.

Today, researchers from the University of Sydney, the Brain and Mind Research Institute, the George Institute for Global Health, and the University of Cambridge are following the vascular explanation to lead a world-first effort to prevent dementia.

Using a suite of new electronic and web-based interventions, they will soon commence a massive trial of low cost, high impact interventions targeting dementia risk factors in 40,000 people aged 50 to 80 years.

"Many preclinical, neurodegenerative changes in the brain occur for at least a decade before dementia symptoms become fully apparent. Therefore, it is vital that we address dementia risk factors before people show signs of brain degeneration and cognitive impairment that are on the slippery slope to dementia," says the University of Sydney's Sharon Naismith, who will lead the trial.

While the researchers hope the range of interventions on offer will largely slow or delay the onset of dementia among 40,000 people initially targeted to participate in the research trial, those who begin showing signs of cognitive impairment will be offered more intensive, targeted treatments

One great irony remains.

The great achievements that have been made in preventing millions of deaths from coronary heart disease and stroke in recent decades have extended the average human lifespan well into the mid-80s, in western societies.

But by 2050, dementias of all kinds will engulf more than 100 million people across the globe. In our effort to forestall disease, ageing and death, especially from heart disease and stroke, we may be unleashing a tsunami of people destined for age-related dementia, particularly if the vascular explanation holds true.

Jonathan Stone puts it this way: "We know that the biggest risk factor for dementia is age; put sardonically, the surest way to avoid dementia is to die young."

Provided by University of Sydney