A stroke of genius

With over 600 scholarly articles and 23,000 citations to his name, Professor Vladimir Hachinski has been at the forefront of stroke, sudden death and vascular cognitive impairment research for the last 40 years.

In reality, vascular disease does not involve the brain to such an extent, and when dementia occurs it is often on the background of already existing Alzheimer’s disease (AD). Thus, it is the co-occurrence and interaction of vascular disease and AD that is most commonly responsible for cognitive impairment in the elderly. Moreover, the term vascular cognitive impairment can be defined as any cognitive impairment caused by, or associated with, vascular factors.

This approach is promising as it emphasises the one component that we can now treat and prevent, which is the vascular one.

Another key area of your research is the incidence of sudden death following stroke. Firstly, why does this occur, and secondly, why are right-handed individuals more susceptible?

The incidence of sudden death after stroke varies according to the severity. The more severe the stroke, the more likely it is to happen. With that said, it can also occur in individuals with mild stroke and those who are recovering from stroke.

As for the higher incidence for right-handed individuals, we are not entirely certain of the reason. The likelihood is that in strongly right-handed individuals the dominance of the right insula of the brain for sympathetic activities is probably greater than that in left-handers (and ambidextrous individuals), where the dominance is more distributed between the two insulas. Thus, if one insula is then damaged, the imbalance is much greater if sympathetic function is largely one-sided. From this, we have hypothesised that the origin of the fatal arrhythmias is an imbalance between the sympathetic and parasympathetic systems.

Your more recent research concerns AD and, in particular, its relationship with stroke. What are the implications of this study?

We have shown experimentally that compared to control animals amyloid deposits (a hallmark of AD) are larger and grow after the occurrence of stroke. Similarly, inflammation is greater and flares. Experimental treatment can suppress brain changes and the cognitive consequences.

If we confirm this clinically, it will allow clinicians worldwide to use a joint treatment of anti-amyloid and anti-inflammatory agents to reduce the impact and mitigate the effects of stroke. It will also delay AD in those who might have become prone to it by the infarct. This has tremendous implications given that by the age of 73 around 50 per cent of the general population will have amyloid accumulations within the brain.

Our plans include a multidisciplinary attack on the problem. We are undertaking an epidemiological study in collaboration with the Karolinska Institute in Stockholm and are collaborating with a number of centres on both the clinical and experimental side.

Finally, could you highlight your work on stroke prevention?

My colleague Dr Richard Chan and I lead a Canada-wide study on stroke prevention. It is based on the premise that in order to control blood pressure, weight reduction and other risk factors we need to change human behaviour. *We believe that the most powerful agent in accomplishing this is another caring human being.*

A preliminary study has shown that a layperson working with the patient is often a more effective strategy for reducing high blood pressure and body weight than the usual care provided by a doctor or nurse. The Canada-wide study will provide definitive answers to the question and, if positive, could lead to an effective, low-cost intervention that might be applied worldwide, helping to not only prevent stroke and cognitive deterioration, but heart attacks and renal failure.
Understanding vascular mechanisms

The world of age-related pathologies is expanding and now, more than ever, there is a need for novel treatment, prevention and management strategies. Pioneering research undertaken in Canada and Sweden seeks to prevent stroke, delay Alzheimer’s disease and enhance brain health.

According to the World Heart Federation, 15 million people suffer stroke worldwide each year. In the US alone, more than 140,000 people die annually from stroke. Not always fatal, it is the second leading cause of serious long-term disability, after dementia. While the incidence of stroke is declining in developed countries, largely due to efforts to reduce blood pressure and smoking, the ageing population means that overall rates remain high. Indeed, studies show that the risk of stroke doubles for each decade between the ages of 55 and 85.

A stroke is a sudden loss of brain function. It is caused by the interruption of flow of blood to the brain (ischaemic stroke) or the rupture of blood vessels in the brain (haemorrhagic stroke). The interruption of blood flow or the rupture of blood vessels causes brain cells (neurons) in the affected area to die. After a stroke, it is known that there is an increase in the production of the toxic amyloid beta (Aβ) peptides that are believed to cause Alzheimer’s disease. Certainly, neuroscientists are aware of the escalated risk of Alzheimer’s disease (AD) in people who have had a stroke.

Dr Vladimir Hachinski is Professor of Neurology and Epidemiology, and Distinguished University Professor at Western University in Ontario, Canada. His primary objectives are to prevent stroke, delay AD and enhance brain health through integrated, synergetic, population, experimental and clinical studies. An international leader, his career spans more than 40 years and his contributions to the fields of stroke, vascular cognitive impairments and brain-heart interactions have seen him indirectly save and improve millions of lives on a worldwide scale.

Vascular mechanisms

Hachinski began his career researching migraines, publishing detailed descriptions of the visual symptoms experienced by 100 children who were prone to the condition. At the time, it was thought that migraine pain was caused by dilation of the brain’s blood vessels, but Hachinski – along with Professor John W Norris and Drs Perry Cooper and John Edmeads – demonstrated that pain could be relieved by ergotamine without changing the calibre of the brain’s blood vessels. These findings led the migraine research community to refocus on the extracranial circulation.

Having studied the vascular mechanisms of migraine, Hachinski turned his attention to the treatment of stroke patients. Alarmed by the lack of emphasis on urgency, he introduced the term ‘brain attack’. Now in common usage, the term reflects the need to act swiftly, mobilising both medical professionals and, more importantly, the general public.

Moreover, his collaboration with Norris led to the establishment of the world’s first successful acute stroke unit in Toronto in the 1970s and later in London, Ontario. Their acute stroke units contain dedicated and specialised healthcare workers that benefit the patients on multiple levels and ultimately save lives, as Hachinski explains: “The key to stroke units is concentrating stroke patients in one physical location. This results in close interactions with all those concerned and leads to expertise being shared within the same environment”.

Stroke-related research

Leukoaraiosis describes the changes observed in white matter seen in the brain scans of elderly patients. These abnormalities are detected more frequently among patients with strokes and vascular dementia, and the term was coined by Hachinski in a 1986 paper to emphasise that both the clinical relevance and pathogenesis of the condition were unknown at the time. The origins of the word are Greek, namely the combination of leuko- (meaning ‘white’) and ariaos (meaning diminution of density). The many causes include small vessel infarcts in the sub-cortical white matter.

Following this work, Hachinski focused much of his research on a phenomenon known as cerebrogentic sudden death (CSD). Caused by fatal cardiac arrhythmias, it has long been noted that stroke can lead to an increased risk of developing CSD and this was something Hachinski and his fellow collaborators were keen to examine further. Indeed, the group – which included Norris, and Drs Martin Myers, Gordon Froggat and Michael Sole – observed that some patients recovered from stroke only to die suddenly for no apparent reason.

In an important study undertaken in 1992 with Drs David Cechetto and Stephen Oppenheimer, Hachinski identified the role of a specialised brain region, known as the insula, in stroke-induced cardiovascular disturbances. These disturbances included electrocardiographic changes, a known arrhythmia associated with CSD. This breakthrough study has meant that the efforts of researchers in the field who are examining post-infarction CSD have now
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Professor Vladimir Hachinski is a Distinguished Professor and past Richard and Beryl Ivey Chair of the Department of Clinical Neurological Sciences at Western University, Canada. Together with Professor John W Norris, he established the world’s first successful acute stroke unit. He also discovered, in collaboration with Dr David Cechetto, the brain’s insula role in sudden death and a link between Alzheimer’s disease and stroke, paving the way for new treatments. Hachinski is the first Canadian President of the World Federation of Neurology, the Founding Chair of the Working Group, World Brain Alliance, and a recipient of the Order of Canada. Formerly, he was also the Editor-in-Chief of the journal Stroke, the leading publication in the field.

In 2005, Hachinski, in collaboration with Drs Shawn Whitehead and David Cechetto, presented an attractive, synergistic theory for this using a rat model of cerebral ischemia. It is hypothesised that these mechanisms might play a meditative role between AD and stroke.

The team used a rat model of cerebral ischaemia, along with histochemical and immunohistochemical analyses which are employed to examine the chemical composition of the cells and tissues. Hachinski and his colleagues demonstrated that there was an enhanced inflammatory response in animals with amyloid-beta (a component of AD pathology) toxicity and ischaemia. This critical finding holds much promise in a clinical setting as an anti-inflammatory and anti-amyloid treatment that might mitigate deficits associated with this deadly combination of pathologies.

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These are just a few examples of Hachinski’s studies that have made substantial contributions to the field of vascular research and associated pathologies. Over the course of his career, his work on vascular cognitive impairment, stroke and brain-heart interactions has helped to delay or avoid cerebral vascular disease.

Further to this, Hachinski’s collaborative research has changed the way the public and clinicians approach stroke. It is now understood that swift action must be taken at the onset of stroke symptoms to prevent serious damage, and this urgency has been widely publicised in public health initiatives. Similarly, Hachinski’s studies into age-related diseases and their interactions have focused almost entirely on vascular components and it is these components that are treatable and preventable.

The steady shift in demographics in the last few decades now means that humans are living longer than ever before. Thus, understanding and preventing pathologies associated with ageing is becoming more relevant for healthcare services and individuals alike.