Scientists make surprising finding in stroke research

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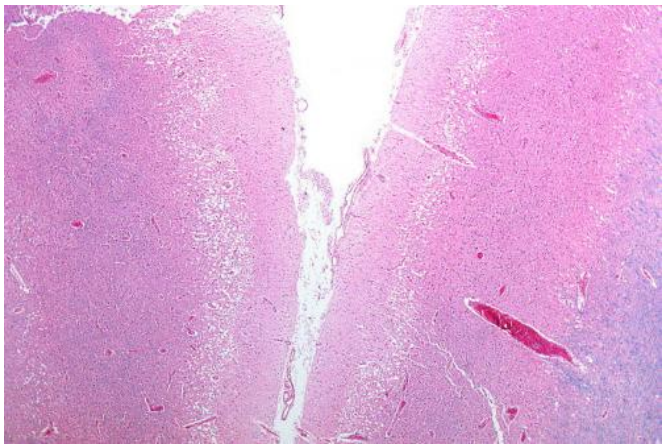

Micrograph showing cortical pseudolaminar necrosis, a finding seen in strokes on medical imaging and at autopsy. H&E-LFB stain. Credit: Nephron/Wikipedia

Scientists at The University of Manchester have made an important new discovery about the brain's immune system that could lead to potential new treatments for stroke and other related conditions.

Inflammation is activated in the brain after a stroke, but rather than aiding recovery it actually causes and worsens damage. That damage can be devastating. In fact, stroke is responsible for 10% of deaths worldwide and is the leading cause of disability.

Therefore, understanding how inflammation is regulated in the brain is vital for the development of drugs to limit the damage triggered by a stroke.

Dr David Brough from the Faculty of Life Sciences, working alongside colleagues including Professors Dame Nancy Rothwell and Stuart Allan, has studied the role of inflammasomes in stroke. These inflammasomes are large protein complexes essential for the production of the inflammatory protein interleukin-1. Interleukin-1 has many roles in the body, and contributes to cell death in the brain following a stroke.

Dr Brough explains: "Very little is known about how inflammasomes might be involved in brain injury. Therefore we began by studying the most well researched inflammasome NLRP3, which is known to be activated when the body is injured. Surprisingly we found that this was not involved in inflammation and damage in the brain caused by stroke, even though drugs are being developed to block this to treat Alzheimer's disease."

Further studies using experimental models of stroke demonstrated that it was actually the NLRC4 and AIM2 inflammasomes that contribute to brain injury, rather than NLRP3.

This discovery was unexpected, since NLRC4, was only known to fight infections and yet Dr Brough and colleagues found that it caused injury in the brain. This new discovery will help the Manchester researchers discover more about how inflammation is involved in brain injury and develop new drugs for the treatment of stroke.

The research was funded by the Wellcome Trust and Medical Research Council and has been published in *PNAS*.

As well as identifying new targets for potential drug treatments for stroke Dr Brough points out how little we currently know about how the immune system works in the brain.

He says: "We know very little about how the immune system is regulated in the brain. However, its important we understand this since it contributes to disease and injury. For example, in addition to stroke, Alzheimer's disease has an inflammatory aspect and even depression may be driven by inflammation."

More information: AIM2 and NLRC4

inflammasomes contribute with ASC to acute brain injury independently of NLRP3 , *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1419090112

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