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Study details brain damage triggered by mini-strokes

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A new study appearing today in the *Journal of Neuroscience* details for the first time how "mini-strokes" cause prolonged periods of brain damage and result in cognitive impairment. These strokes, which are often imperceptible, are common in older adults and are believed to contribute to dementia.

"Our research indicates that neurons are being lost as a result of delayed processes following a mini-strokes that may differ fundamentally from those of acute ischemic events," said Maiken Nedergaard, M.D., D.M.Sc., the lead author of the study and professor of Neurosurgery at the University of Rochester Medical Center (URMC). "This observation suggests that the therapeutic window to protect cells after these tiny strokes may extend to days and weeks after the initial injury."

The prevalence of mini-strokes, or microinfarcts, has only been recently appreciated because common imaging techniques, such as MRI, are typically not sensitive enough to detect these microscopic injuries.

Similar to severe ischemic strokes, mini-strokes are caused when blood flow is blocked to a small area of the brain, usually by particle that travelled there from another part of the body. But unlike acute ischemic strokes – which bring about immediate symptoms such as numbness, blurry vision, and slurred speech – mini-strokes usually pass without notice. However, it is increasingly appreciated that these smaller strokes have a lasting impact on neurological function.

Microinfarcts are far more common than previously understood; it is believed that about 50 percent of individuals over the age of 60 have experienced at least one mini-stroke. Studies have also correlated the presence of mini-strokes with the symptoms of dementia. An estimated 55 percent of individuals with mild dementia and upwards of 70 percent of individuals with more severe symptoms show evidence of past mini-strokes. This association has led researchers to believe that these mini-strokes may be key contributors to age-related cognitive decline and dementia.

Nedergaard and her colleagues were the first to develop an animal model in which the complex progression and, ultimately, the cognitive impact of mini-strokes could be observed. Her team found that, in most instances, these strokes result in a prolonged period of damage to the brain.

A small fraction of these microinfarcts unfold in a manner similar to acute strokes; cell death is immediate and the brain quickly seals off the site of the stroke and begins to "digest" the damaged tissue. However, the researchers also identified a second and far more common form of mini-stroke – which they labeled incomplete lesions – where the cell death can drag on for several weeks.

"In most microinfarcts the injury is incomplete," said Nedergaard. "There is no scar tissue to separate the stroke site from the rest of the brain and the cells that would normally support the neurons may not function properly. As a result, the neurons at the site continue to slowly die like a smoldering fire. This suggests that, unlike acute ischemic strokes where the cell death occurs in the first 24 hours, there is a longer period in which we can medically intervene and stop the neuronal death that results from mini-strokes."

The researchers then attempted to determine the cognitive impact of

microinfarcts. Mice who were victims of mini-strokes underwent a series of experiments during which they had to recall objects or respond to certain audio cues. The researchers observed that the mice with mini-strokes were far more likely to fail these tasks – suggesting neurological impairment – compared to healthy mice.

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