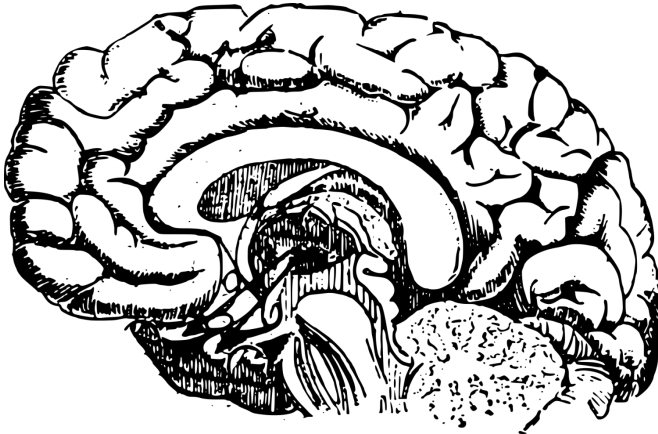


# Researchers discover cause of brain sensitivity to lack of oxygen

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Researchers at Maastricht University Medical Center and Maastricht University have discovered why the brain is more sensitive to oxygen deprivation, or hypoxia, than other organs. Hypoxia caused by a stroke, for example, activates a specific mechanism that is protective in other organs but can be detrimental to the brain. 'This discovery solves a long-standing mystery of the unique sensitivity of the brain to hypoxia,' says head researcher and professor Harald Schmidt. The research results were published today in the leading scientific journal *Proceedings of the National Academy of Sciences*.

In most cases, a stroke is caused by a blocked artery in the brain, which deprives the brain of oxygen. To prevent [brain death](#), the blood clot must be dissolved with an anticoagulant or removed via a catheter. Stroke victims that survive are left with detrimental symptoms, regardless of how quickly they were treated. These symptoms may include severe paralysis and speech disorders.

## Self-destruction

An enzyme was found to play a crucial and specific role during a stroke. Following oxygen deprivation, this enzyme, known as NOX4, is produced by several organs and muscles. In all investigated cases, however, NOX4 is harmless, with one notable exception: the production of NOX4 in the brain is disastrous. How this happens is now clear down to the cellular level. First, the enzyme triggers the breakdown of cells of the [blood-brain barrier](#), which protects the brain against blood and other components. Second, NOX4 also triggers a self-destruction mechanism in neurons. This combined effect results in physical and mental problems. When the NOX4 gene is deleted or the NOX4 enzyme inhibited with drugs, the blood-brain barrier and neurons remain intact and brain damage is prevented.

## Therapy

This important finding opens new doors for treating post-stroke brain damage. "We've known for some time that [oxygen deprivation](#) leads to brain damage, we just never knew why. The crucial role the NOX4 enzyme plays will help us develop new treatment options to protect the [brain](#) after a stroke.' With the help of a proof-of-concept grant provided by the European Research Council the Maastricht researchers are already one step further by developing drugs that are capable of inhibiting the disastrous effects of this [enzyme](#) as soon as possible for patient therapy.

**More information:** Ana I. Casas et al., "NOX4-dependent neuronal autotoxicity and blood-brain barrier breakdown explain the superior sensitivity of the brain to ischemic damage," *PNAS* (2017).

[www.pnas.org/cgi/doi/10.1073/pnas.1705034114](http://www.pnas.org/cgi/doi/10.1073/pnas.1705034114)

Provided by Maastricht University Medical Center

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