

Mouse studies suggest daily dose of ginkgo may prevent brain cell damage after a stroke

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Working with genetically engineered mice, researchers at Johns Hopkins have shown that daily doses of a standardized extract from the leaves of the ginkgo tree can prevent or reduce brain damage after an induced stroke.

The scientists, in a report published in *Stroke*, say their work lends support to other evidence that *ginkgo biloba* triggers a cascade of events that neutralizes free radicals known to cause cell death.

"It's still a large leap from rodent brains to human brains but these results strongly suggest that further research into the protective effects of ginkgo is warranted," says lead researcher Sylvain Doré, Ph.D., an associate professor in the Department of Anesthesiology and Critical Care Medicine. "If further work confirms what we've seen, we could theoretically recommend a daily regimen of ginkgo to people at high risk of stroke as a preventive measure against brain damage."

In the study, researchers gave *ginkgo biloba* EGb 761 - a lab-quality form of the extract - to normal mice and HO-1 knockout mice, mice lacking the gene that produces the enzyme heme oxygenase-1(HO-1). HO-1 breaks down heme, a common iron molecule found in blood, into carbon monoxide, iron and biliverdin. HO-1 has been shown to act as an antioxidant and have a protective effect against inflammation in animal models.

Doré and his team gave 100 milligrams per kilogram of EGb 761 extract

orally once daily for seven days before inducing stroke in the mice by briefly blocking an artery to one side of the brain.

After stroke induction, the mice were tested for brain function and brain damage. One such test, for example, involves running patterns, another tests reaction to an external stimulus. Similar tests were conducted on mice that did not receive the ginkgo extract.

Neurobehavioral function was evaluated before the study and at 1, 2 and 22 hours after stroke using a four-point scale: (1) no deficit, (2) forelimb weakness, (3) inability to bear weight on the affected side, (4) no spontaneous motor activity.

Results showed that normal mice that were pretreated had 50.9 percent less neurological dysfunction and 48.2 percent smaller areas of brain damage than untreated mice. These positive effects did not exist in the HO-1 knockout mice.

"Our results suggest that some element or elements in ginkgo actually protect brain cells during stroke," says Doré.

Roughly 700,000 people experience a stroke in the United States annually. Of those, 87 percent have an ischemic stroke, which is caused by a blocked artery in the brain. Some brain damage occurs simply from the lack of blood getting to brain cells; however, it is known that an increase in the presence of free radicals at the site of an ischemic stroke - once the clot is cleared and the blood supply returns - is also a major cause of resulting brain cell damage. Free radicals are toxic oxygen molecules that are produced when cells die. According to Doré and his team, ginkgo increases HO-1 levels, and the antioxidant properties of this enzyme eliminate free radicals at the surrounding regions of the stroke site.

The only current treatment for ischemic stroke is to clear the clot with tissue plasminogen activator (tPA) or other means. This, however, offers no real protection against the cell damage that occurs when blood flow is restored.

"Ginkgo has long been touted for its positive effects on the brain and is even prescribed in Europe and Asia for memory loss," says Doré. "Now we have a possible understanding for how ginkgo actually works to protect neurons from damage."

Native to China, the ginkgo tree is grown as an ornamental shade tree in Australia, Southeast Asia, Europe, Japan and North America. It is commercially cultivated in France and the United States. It has a grey bark, reaches a height of 35 meters and a diameter of 3 to 4 meters. It has deciduous, fan-like leaves that are green, grey-yellow, brown or blackish.

Source: Johns Hopkins Medical Institutions

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