# Common food dye may hold promise in treating spinal cord injury

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A common food additive that gives M&Ms and Gatorade their blue tint may offer promise for preventing the additional - and serious - secondary damage that immediately follows a traumatic injury to the spinal cord. In an article published online today in the *Proceedings of the National Academy of Sciences,* researchers report that the compound Brilliant Blue G (BBG) stops the cascade of molecular events that cause secondary damage to the spinal cord in the hours following a spinal cord injury, an injury known to expand the injured area in the spinal cord and permanently worsen the paralysis for patients.

This research builds on landmark laboratory findings first reported five years ago by researchers at the University of Rochester Medical Center. In the August 2004 cover story of Nature Medicine, scientists detailed how ATP, the vital energy source that keeps our body's cells alive, quickly pours into the area surrounding a spinal cord injury shortly after it occurs, and paradoxically kills off what are otherwise healthy and uninjured cells.

This surprising discovery marked a milestone in establishing how secondary injury occurs in spinal cord patients. It also laid out a potential way to stop secondary spinal injury, by using oxidized ATP, a compound known to block ATP's effects. Rats with damaged spinal cords who received an injection of oxidized ATP were shown to recover much of their limb function, to the point of being able to walk again, ambulating effectively if not gracefully.

Now, scientists detail the clearing of yet another hurdle in moving this research closer from bench to bedside by successfully identifying a compound that could be administered systemically to achieve the same benefit. Previously, the team needed to inject a compound directly into the injured spinal cord area to achieve its results.

"While we achieved great results when oxidized ATP was injected directly into the spinal cord, this method would not be practical for use with spinal cord-injured patients," said lead researcher Maiken Nedergaard, M.D., D.M.Sc., professor of Neurosurgery and director of the Center for Translational Neuromedicine at the University of Rochester Medical Center. "First, no one wants to put a needle into a spinal cord that has just been severely injured, so we knew we needed to find another way to quickly deliver an agent that would stop ATP from killing healthy motor neurons. Second, the compound we initially used, oxidized ATP, cannot be injected into the bloodstream because of its dangerous side effects."

Nedergaard cautions that while this body of work offers a promising new way of treating spinal cord injury, it is still years away from possible application in patients. In addition, any potential treatments would only be helpful to people who have just suffered a spinal cord injury, not for patients whose injury is more than a day old. Just as clot-busting agents can help patients who have had a stroke or heart attack who get to an emergency room within a few hours, so a compound that could stem the damage from ATP might help patients who have had a spinal cord injury and are treated immediately.

## Too Much of a Good Thing

While ATP is usually considered to be helpful to our bodies - after all, it's the main source of energy for all of our body's cells - Nedergaard was the first to uncover its darker side in the spinal cord. Immediately

after a spinal cord injury occurs, ATP surges to the damaged area, at levels hundreds of times higher than normal. It is this glut of ATP that over-stimulates neurons and causes them to die from metabolic stress.

Neurons in the spinal cord are so susceptible to ATP because of a molecule known as "the death receptor." Scientists know that the receptor - called P2X7 - plays a role in regulating the deaths of immune cells such as macrophages, but in 2004, Nedergaard's team discovered that P2X7 also is carried in abundance by neurons in the spinal cord. P2X7 allows ATP to latch onto motor neurons and send them the flood of signals that cause their deaths, worsening the spinal cord injury and resulting paralysis.

So the team set its sights on finding a compound that not only would prevent ATP from attaching to P2X7, but could be delivered intravenously. In a fluke, Nedergaard discovered that BBG, a known P2X7R antagonist, is both structurally and functionally equivalent to the commonly used FD&C blue dye No. 1. Approved by the Food and Drug Administration as a food additive in 1982, more than 1 million pounds of this dye are consumed yearly in the U.S.; each day, the average American ingests 16 mgs. of FD&C blue dye No. 1.

"Because BBG is so similar to this commonly used blue food dye, we felt that if it had the same potency in stopping the secondary injury as oxidized ATP, but with none of its side effects, then it might be great potential treatment for cord injury," Nedergaard said.

The team was not disappointed. An intravenous injection of BBG proved to significantly reduce secondary injury in spinal cord-injured rats, who improved to the point of being able to walk, though with a limp. Rats that had not received the BBG solution never regained the ability to walk. There was one side effect: Rats who were injected with BBG temporarily had a blue tinge to their skin.

Nedergaard's long-time collaborator on this and other projects, chair of the University of Rochester Department of Neurology Steven Goldman, M.D., Ph.D., adds, "We have no effective treatment now for patients who have an acute spinal cord injury. Our hope is that this work will lead to a practical, safe agent that can be given to patients shortly after injury, for the purpose of decreasing the secondary damage that we have to otherwise expect."

Nedergaard and Goldman believe that further laboratory testing will be needed to test the safety of BBG and related agents before human clinical trials could begin. Nonetheless, the investigators are optimistic that with sufficient study, strategies like this could yield new treatments for acute spinal cord injuries within the next several years.

Source: University of Rochester Medical Center (news : web)