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Researchers Discover How Folate Promotes Healing In Spinal Cord Injuries

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(PhysOrg.com) -- The vitamin folate appears to promote healing in damaged rat spinal cord tissue by triggering a change in DNA, according to a laboratory study funded by the National Institutes of Health.

The researchers showed that the healing effects of the vitamin increased with the dosage, until regrowth of the damaged tissue reached a maximum level. After this threshold was reached, regrowth declined progressively with increasing doses until it reached the level seen in the absence of the vitamin.

Specifically, folate stimulated a process known as DNA methylation, a natural biochemical process in which chemical compounds known as methyl groups are attached to DNA. The study results suggest that a greater understanding of the chemical sequences associated with folate metabolism and DNA methylation may lead to new techniques to promote healing of damaged spinal cords and other nervous system injuries.

The research is at an early stage and additional studies are needed to determine what role folate might play in the treatment of human beings with spinal cord injury. Information about folate in human nutrition, including dietary sources of the vitamin and appropriate daily intake is available from the folate fact sheet of the NIH Office of Dietary Supplements.

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National Institute of Child Health and Human Development, National Institute of Diabetes and Digestive and Kidney Diseases, National Institute of Dental and Craniofacial Research, and National Institute of Neurological Disorders and Stroke. The findings were published in the Journal of Clinical Investigation.

The addition of methyl groups to alter the functioning of DNA is part of the relatively new field of epigenetics—changing the functioning of DNA without changing the composition of genes. Initially, the only known way a gene's functioning changed was through mutation, a chemical change to the gene itself, explained Bermans J. Iskandar, of the University of Wisconsin-Madison.

"The ability to change gene function through DNA methylation suggests exciting new prospects for understanding the origins of disease and for developing new treatments," Dr. Iskandar said. "Our study showed that folate, a commonly available dietary supplement known to change gene functioning, did so in a way that fosters nervous system repair."

Nearly 11,000 Americans experience a spinal cord injury each year, according to the Centers for Disease Control and Prevention. The effects of spinal cord injury vary with the extent of the injury, with severe injuries resulting in complete paralysis below the injury site.

Folate, a B vitamin, occurs naturally in leafy green vegetables and other foods. The synthetic form, folic acid, is used to supplement cereal grains in the United States. The vitamin is important for the formation of the brain and spinal cord in the early embryo. The U. S. Public Health Service recommends that all women of childbearing age consume 400 micrograms of folic acid each day to reduce their risk of having a child with a neural tube defect, a birth defect of the brain and spinal cord.

Because of folate's role in fetal spinal cord development, the researchers

sought to determine if the vitamin could promote healing in damaged adult nervous system tissue. In a previous study, the researchers showed that folate could enhance the regrowth of axons, or nerve fibers, in rats with spinal cord injuries.

In the current study, they measured folate's effects at various doses. They found that as the dose increased, so did the amount of axon regrowth.

"Interestingly, the more folate we gave, the more regrowth we saw, eventually achieving almost a tenfold increase in axonal regeneration," Dr. Iskandar said. Beyond the peak dose of 80 micrograms per kilogram of body weight, the effect decreased but without causing toxicity or nerve damage.

To understand how folate helps repair damaged axons, the researchers undertook additional observations. They found that injured nerve tissue began producing surface receptors for folate. Folate fits into the receptors, like a key fits into a lock, and then is absorbed into the nerve cell. After folate was absorbed into injured nervous system tissue, the nerve cells began producing enzymes that attach methyl groups to DNA. Chemically blocking folate from binding to the nerve cells, or blocking the methylation enzymes, hindered the nerve healing process.

"Injuring the spinal cord seems to enhance its ability to receive folate in its cells," Dr. Iskandar said.

The researchers also tested the methylation of spinal cord DNA at various doses of folate and found that, like the regrowth of axons, DNA methylation peaked at a dose of 80 micrograms folate per kilogram of body weight.