

Natural Chemical Found in Strawberries Boosts Memory in Healthy Mice

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Mothers have long exhorted their children to eat their fruit and vegetables. But once kids are beyond mom's watchful eye, the hated greens often go the way of Barbie dolls and power rangers. Now, there's another reason to reach for colorful fruits past adolescence.

Fisetin, a naturally occurring flavonoid commonly found in strawberries and other fruits and vegetables, stimulates signaling pathways that enhance long-term memory, report researchers at the Salk Institute for Biological Studies in this week's Online Early Edition of the *Proceedings of the National Academy of Sciences*.

Roughly one third of people age 60 and over suffer from memory and recall woes. As the average age of the U.S. population climbs, the number of people ravaged by Alzheimer's disease and other forms of dementia continues to rise.

"Since the development of a basic understanding of the biochemical pathways involved in memory formation, the holy grail of CNS research in the pharmaceutical industry is the identification of a safe, orally active drug that activates memory-associated pathways and enhances memory," says lead author Pamela Maher, Ph.D., a researcher in the Cellular Neurobiology Laboratory at the Salk Institute.

Maher hit upon the beneficial effects of fisetin when she screened a collection of flavonoids, substances with anti-oxidant activities found in many plants, for their neuroprotective abilities in tissue culture models

of neurodegenerative disease.

Maher found that some of those compounds, including fisetin, induced differentiation or maturation of neural cells. Maher explains, “That suggested to us that these compounds might be particularly beneficial, since they might not only protect neural cells from dying but might be able to promote new connections between nerve cells.”

Interestingly the signaling pathway activated by fisetin in neural differentiation also played a role in memory formation, a process neuroscientists call “long-term potentiation” or LTP. LTP allows memories to be stored in the brain by strengthening connections between neurons. “We wanted to find out whether we could detect any effects of fisetin on long-term potentiation and the formation of memories in animals,” Maher recalls.

Since the hippocampus plays an important role in establishing new memories, Maher, and co-authors Tatsuhiro Akaishi and Kazuho Abe, both at Musashino University in Tokyo, Japan, extended the study and found that fisetin activates the same signaling pathway in rat hippocampal tissues and also induces LTP.

Next, they tested fisetin’s effects in a so-called object discrimination test in mice. The mice get to explore two objects for a certain amount of time. The next day, one of the objects is replaced with a novel one. If the mice remember the object from the day before, they spend less time exploring the old one and instead turn their attention to the novel object. Indeed, mice administered a single dose of fisetin could better recall familiar objects. In fact, fisetin worked almost as well as rolipram, a substance known to enhance memory.

Memory loss caused by neurodegenerative disease occurs due to loss of neurons, a situation very different from that of healthy mice. Thus the

ultimate goal is to stop neuronal loss. Nevertheless, memory-enhancing drugs can improve Alzheimer's disease symptoms.

The observations that fisetin protects and promotes survival of cultured neurons and boosts memory in healthy mice make it a promising candidate for further studies. Notes Maher, "This is the first time that the function of a defined natural product has been characterized at the molecular level in the central nervous system and also shown to enhance both LTP in vitro and long-term memory in vivo."

"The good news is that fisetin is readily available in strawberries but the bad news is that because of its natural product status there may be little financial interest in getting it into human clinical trials for diseases associated with memory loss such as Alzheimer's, where the treatment options are currently very limited," says Maher.

Besides strawberries, fisetin is found in tomatoes, onions, oranges, apples, peaches, grapes, kiwifruit and persimmons. Gingko biloba leaves, while rich in other flavonoids, do not contain fisetin.

While eating strawberries sounds like an enjoyable alternative to popping a pill, Maher cautions that it would take about 10 pounds a day to achieve a beneficial effect, which might prove too much even for the most avid strawberry lovers.

Source: Salk Institute for Biological Studies

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