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Cocoa Flavanols May Reverse Age-Related Memory Decline

Liam Davenport | |October 28, 2014

Age-related memory decline may be reversed with high doses of naturally occurring cocoa flavanols, US researchers have discovered in findings that establish the dentate gyrus as central to cognitive decline.

"Together, these results provide evidence that age-related changes in the DG [dentate gyrus] observed in aging humans underlie and drive a hippocampal-dependent component of cognitive aging," the investigators write.

Discussing the motivation for the study, lead researcher Scott Small, MD, Boris and Rose Katz Professor of Neurology and director of the Alzheimer's Disease Research Center in the Taub Institute at Columbia University Medical Center, in New York City, told *Medscape Medical News*: "Over the last 10 years or so, there have been a lot of observational studies that have suggested that the dentate gyrus, which is a region within the hippocampus, is linked to aging and age-related memory decline."

However, he noted: "That's just been correlational, so the real motivation here was to rely on flavanols, which previous mouse studies have established increase function selectively in the dentate gyrus, and see if we could show that [effect] in humans, in an effort to establish a causal link between the dentate gyrus and aging."

The study was published online October 26 in *Nature Neuroscience*.

Significant Impact

For the study, the team developed a functional magnetic resonance imaging (fMRI) technique that utilized steady-state contrast enhancement to create isolated cerebral blood volume (CBV) maps of the hippocampus. This allows the data to be combined into a single, three-dimensional snapshot, rather than as slices.

Comparing the precise patterns observed in 35 healthy individuals aged 21 to 65 years with those recorded from patients in the preclinical stages of Alzheimer's disease, they were able to develop a precise pattern of age-related dentate gyrus function.

They then combined a computerized modification of the Benton Visual Retention Test, termed ModBent, for use in healthy individuals with a specifically designed task that built on previous research indicating that the dentate gyrus is involved in the pattern separation of visually similar objects.

In a series of experiments with healthy volunteers, the researchers were able to confirm that task performance declined with normal aging, and through use of CBV-fMRI, that this cognitive task's function was localized to the site of age-related dentate gyrus dysfunction.

In the second part of the study, 41 healthy but sedentary individuals aged 50 to 69 years were randomly assigned to either a high flavanol intake of 900 mg cocoa flavanols and 138 mg of (–)- epicatechin per day, with or without aerobic exercise, or a low flavanol intake of 10 mg cocoa flavanols and <2 mg (–)-epicatechin per day, with or without aerobic exercise.

The dietary intervention, which was developed specifically for research purpose by Mars, Inc, using a proprietary process to extract flavanols from cocoa beans, was administered for 3 months. A battery of neuropsychological tests, including the ModBent, and an MRI scan were administered before and after the intervention.

Analysis revealed that, independent of exercise, ModBent performance improved significantly among individuals randomly assigned to the high-flavanol intervention, at a reaction time of 1997 ms vs 2627 ms in the low-flavanol

group (P = .038). The high-flavanol intervention was associated with a mean improved cognitive performance of 630 ms.

High-flavanol recipients also had a significant increase in CBV in the dentate gyrus compared with individuals assigned to the low-flavanol intervention. This increase was associated with changes in performance on the ModBent.

Exercise, unexpectedly, had no impact on the outcomes.

Not in a Candy Bar

Commenting on the findings for *Medscape Medical News*, Keith Fargo, PhD, director of scientific programs and outreach at the Alzheimer's Association, was keen to stress that the study was not about consuming flavanols from chocolate, despite the investigators having used a cocoa derivative. He said: "You are not going to go down to your supermarket and get this in a candy bar!"

Dr Fargo added: "The other thing that's really important about this article to remember is that it's not about Alzheimer's disease either. This is specifically about cognitive decline in normal aging."

"Alzheimer's disease is not just memory problems, it is a fatal brain disease, and the Alzheimer's Association is very interested in making sure that the scientific community has the tools that they need to properly understand the difference between Alzheimer's disease and normal cognitive decline.... From that standpoint, we think it's an interesting and informative study," he said.

Dr Fargo also emphasized that it is too early to be able to draw firm conclusions from the study findings. Describing it as "extremely preliminary," he noted that it is based on a small sample size and focuses on answering a specific question with a specific cognitive test.

"This cognitive test is not a test of overall cognitive function," he said. "It's not a test of memory. It's a test that is very specifically calibrated to look at the function of the dentate gyrus."

He noted: "Even though this study was designed as a clinical trial in a technical sense of the term, it's not really designed to show that this kind of intervention would be useful in cognitive aging in the general population."

Dr Fargo continued: "This study is really designed to answer a very specific question, which is: If you can boost the activity in the dentate gyrus, will you see increases in the cognitive functions that are served by the dentate gyrus?"

Dr Small and colleagues are keen to investigate further the impact of flavanols on dentate gyrus function. "We are gearing up to another study, not just to replicate in a larger sample but also to understand what's the minimum amount of these flavanols you need."

"Perhaps in a future study, we can show that 200 mg are enough, and not necessarily chocolate but maybe a dietician could think of a combination of vegetables and teas and mixes that can be effective," he added.

"That's one way that I think that might work. Another way is that companies like Mars and others might come up with a formulation that is commercially available."

The cocoa flavanol–containing test drink was produced by the food company Mars, Inc, which also partly supported the research. Dr Small and Dr Fargo report no relevant financial relationships.

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