Water's unexpected role in blood pressure control

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Name a drink that can make you more alert for late-night studying, prevent you from fainting after giving blood, and even promote a teensy bit of weight loss.

Chances are you didn't say water. But that's the right answer.

Researchers at Vanderbilt University Medical Center have shown that ordinary water - without any additives - does more than just quench thirst. It has some other unexpected, physiological effects. It increases the activity of the sympathetic - fight or flight - nervous system, which raises alertness, blood pressure and energy expenditure.

David Robertson, M.D., and colleagues first observed water's curious ability to increase blood pressure about 10 years ago, in patients who had lost their baroreflexes - the system that keeps blood pressure within a normal range.

The observation came as a complete surprise, said Robertson, professor of Medicine, Pharmacology and Neurology.

"We had to unlearn the idea that water had no effect on blood pressure, which is what all medical students had been told until the last couple of years."

Although water does not significantly raise blood pressure in healthy young subjects with intact baroreflexes, the investigators found that it

does increase sympathetic nervous system activity and constrict blood vessels (which prevents pooling of blood in the extremities).

These findings prompted the American Red Cross to conduct a study of water drinking as a method for reducing fainting responses. The study found that drinking 16 ounces of water before blood donation reduced the fainting response by 20 percent.

"This response to water may turn out to be very important for retaining blood donors," Robertson said. "If you pass out after giving blood, you pretty much never give blood again. If we can reduce fainting by 20 percent, we can reduce the unpleasantness of passing out and really bolster the number of people who can continue to be blood donors."

Julia McHugh, a student in Vanderbilt University School of Medicine's Medical Scientist Training Program, tackled the questions of where water is acting, and how, in a series of studies in mice. The team's latest findings are reported in the June issue of the journal *Hypertension*.

McHugh and colleagues found that water introduced directly into the stomach or duodenum (the first part of the small intestine) raised blood pressure, which ruled out an oral or esophageal mechanism for the response. They also tested a similar volume of saline (salt-containing solution). This did not raise blood pressure, which suggested that stretch of the tissues was not part of the mechanism and that perhaps water's lack of salt might be important.

The investigators ultimately determined that water dilutes the plasma in the blood vessels leading away from the duodenum and that this short-lived reduction in salt concentration (hypo-osmolality) is responsible for water's blood pressure-raising (pressor) effect. They implicated a protein called Trpv4 in the mechanism: mice lacking the Trpv4 gene did not have a pressor response to water.

While it is clear that water evokes a pressor response, the normal role for this physiological system is not certain.

Because it raises sympathetic nervous system activity - and consequently energy expenditure - it does promote weight loss, Robertson said.

"I calculated it might be as much as five pounds a year if you drank three 16 ounce glasses of water a day and nothing else changed. This is not going to be the answer to the weight problem in the United States, but it's interesting that activation of the sympathetic system is enough to do that."

McHugh said she found it fascinating that mice and humans share "such a primitive system, and yet we don't know why it's there or what beneficial effects it might have."

The newly discovered system and its molecular mediators - such as Trpv4 - may be targets for blood pressure regulation, particularly in situations of low blood pressure and fainting, the investigators said. The findings also suggest that investigators who use water as a control substance (a "non-drug") in studies may need to take water's pressor effects into account.

Provided by Vanderbilt University Medical Center