

THE WAITING ROOM

THIS WAY IN

CCSVI and Multiple Sclerosis

Research into a possible connection between chronic cerebrospinal venous insufficiency (CCSVI) and multiple sclerosis (MS) is sparking intense interest in the MS community. People with MS are calling for more access to a controversial treatment to correct CCSVI. Some have even traveled to clinics in India and Poland to undergo the unproven treatment, which can cost thousands of dollars.

More than 2,400 people tuned in to a live Web forum on April 14, sponsored by the National Multiple Sclerosis Society and the American Academy of Neurology (AAN), called “What Do We Know About CCSVI?” The forum gave people an opportunity to hear about the research directly from the doctors who developed the theory and conducted initial research into the MS-CCSVI link. These frequently asked questions provide an overview of the issues discussed in the Webinar.

What is CCSVI?

Chronic cerebrospinal venous insufficiency is an abnormality in how blood drains from the brain and the spinal cord, as reported in research published in 2009 by Paulo Zamboni, M.D., and colleagues in the *Journal of Neurology, Neurosurgery & Psychiatry*. Dr. Zamboni is professor of vascular surgery at Italy’s University of Ferrara. His theory is that stenosis (narrowing of the blood vessels) and/or blockages reverse blood flow in the azygous vein, which carries blood from the lower spine, and internal jugular veins, which carry blood from the brain and neck—and that this causes an overload of iron in the brain and spinal cord.

What does it have to do with MS?

The proposed link between CCSVI and MS is that the increased deposition of iron triggers inflammation and lesions in the brain, leading to the degeneration of the myelin sheath surrounding nerves. The degeneration of myelin is considered the cause of MS.

Dr. Zamboni’s study showed what he and his colleagues called a “dramatic association” between MS and blood flow abnormalities in major veins draining from the brain and spinal cord. The 65 people with different types of MS in the study were 43 times more likely to have blockages or stenosis of the veins than the 235



The message from experts: Do not undergo procedures to correct blood flow unless part of a well-designed clinical trial.

controls, as shown by Doppler high-resolution brain scans. The study was blinded, meaning that the ultrasound technicians and physicians interpreting the scans did not know whether the patients had MS or were in the control group, which was comprised of healthy subjects and subjects with other neurologic diseases.

However, the hypothesis that CCSVI is associated with MS is not proven,

says Dr. Robert Zivadinov, M.D., Ph.D., associate professor of neurology at the State University of New York at Buffalo. The treatment for correcting CCSVI, which involves inserting a tiny balloon or stent into narrow or blocked veins in order to improve blood flow, is still being tested. “There are no data at this moment to determine whether this is useful,” says Dr. Zivadinov, who is studying the approach, known in the MS community as the “liberation treatment.”

Furthermore, uncovering an association between people with CCSVI and MS is not the same as discovering that CCSVI causes MS, emphasizes John Corboy, M.D., professor of neurology at the University of Colorado-Denver and co-director of the Rocky Mountain MS Center at Anschutz Medical Campus. Dr. Corboy says the vascular abnormalities, even if replicated by others with similar and different techniques, could be the result rather than the cause of MS.

Dr. Zivadinov says, “Several studies will be needed to prove the real prevalence of CCSVI in MS. The link has to be proven also by correlating MRI, genetic, and clinical characteristics with CCSVI, which is exactly what we are doing.”

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I've heard that people with MS have gotten much better after venoplasty surgery to correct CCSVI. Is that true?

A small, open-label study by Dr. Zamboni, published last year in the *Journal of Vascular Surgery*, evaluated 65 people with various stages of MS who underwent vascular surgery. (In an open-label study, the participants and researchers know which treatment is being administered, which can bias the results.) They reported some positive outcomes, in particular for people with relapsing-remitting MS, the most common form of the disease. People with this form experience unpredictable attacks, in which MS symptoms worsen, followed by periods of

time when they return to normal or near-normal functioning.

Twenty-seven percent of the study participants were relapse-free before surgery, versus 50 percent at 18 months. But restenosis of the jugular veins—associated with later relapse—occurred in nearly half the patients within 18 months.

It's possible, given the nature of relapsing-remitting MS, that some of the patients might have improved temporarily without the treatment, says Aaron E. Miller, M.D., chief medical officer of the National MS Society and director of the MS Center at Mt. Sinai Medical Center.

Dr. Corbo points out that Dr. Zamboni's study did not have

INSPIRING PEOPLE

Brainy Artist Amy Caron

Amy Caron, an artist based in Salt Lake City, UT, has choreographed contemporary dance, taught college classes on dance and film, and competed as an aerial ski jumper for the U.S. Freestyle Ski Team.

She has no science background. But when she found out that New York's Performance Space 122 (P.S. 122) was commissioning work from artists in partnership with someone outside the art world, she thought immediately of V.S. Ramachandran, M.D., Ph.D., a charismatic neuroscientist she'd once seen on TV.

Caron looked up his research on mirror neurons and was fascinated. Mirror neurons fire when a person (or animal) acts, and when the person observes the same action performed by another. "On a basic level, these neurons facilitate mimicking behavior," she explains. "They cross the barrier between self and other. It's a great topic for art."

She wrote up a proposal to work with Dr. Ramachandran and got the gig. Caron thrust herself into the world of neuroscience, reading medical journals, hanging out in Dr. Ramachandran's research lab and discussing his work with him, and even watching two brain surgeries. The result is *Waves of Mu* (pronounced *myew*), a large-



scale installation/performance work. The installation, named after the EEG oscillations that reflect mirror neuron activity, is designed to trigger the mirror neurons of the audience.

The first part of *Waves of Mu* is a "wall-to-wall, floor-to-ceiling representation of neuroanatomy" in vibrant pink, turquoise, red, and orange, Caron says. The atmosphere is festive and stimulating, with champagne and chocolate served to viewers and reggae music blaring loudly. "I designed the experience as a party, with information that's communicated socially," she says.

The second part of the work is a performance with theater, dance, and video. Caron plays the role of an eccentric scientist teaching her audience how neurons

function—in part by evoking a variety of emotional responses. She soothes them with an image of a cat purring loudly, and then disarms them with footage of skiers getting injured.

"Even though nothing's really happening to you, you take on the feeling of what you see," she says.

In addition to P.S. 122, Caron has put on her show at venues in Vermont and Alaska. *Waves of Mu* will run for students in the University of Utah's medical-education program this fall and at Sushi Art in San Diego in fall 2011.

To see more of more of *Waves of Mu*, go to wavesofmu.com. To see more of Caron's other work, go to amycaron.com. —Lisa A. Phillips

COURTESY OF THE ARTIST

NEUROBICS

Flexible Thinking

Can you think of 50 different uses for a

brick? The conventional response is to think of bricks as building blocks. You can use a brick to build a house, a wall, a path, or a mailbox. But this rigid approach won't get you very far.



To think of more uses for a brick you need to think flexibly. Forget the conventional use of a brick and focus instead on its qualities. A brick is hard, so you can use it to break a window. A brick is heavy, so you can use it as a paper weight. A brick is rectangular, so dip it in paint and use it to stamp colored rectangles on paper.

Now try this flexible thinking challenge. In each puzzle below, figure out what the six words on the left have in common that makes them different from the six words on the right. The order of the words does not matter. To solve this puzzle you will have to forget that these words are names of animals, and focus instead on other qualities of the words.

This puzzle is based on Word Sort, a game on the brain fitness web site lumosity.com.

ant	horse	tiger	viper
cow	eagle	panda	skunk
bear	lion	seal	zebra

tiger	seal	lion	walrus
bear	horse	panda	cow
snake	oyster	lizard	clam

tiger	boa	horse	frog
heron	lion	stork	skunk
viper	eagle	toad	goose

a control group and that patients remained on their disease-modifying drug regimen. "Claims of improvement are based only on comparison to patients themselves prior to the procedures," he says. "No one would accept this as evidence of a treatment effect in MS." Indeed, experts emphasize that patients should not stop their current therapies.

Are larger trials underway?

Dr. Zivadinov is trying to duplicate Dr. Zamboni's findings in a larger study designed to examine how prevalent CCSVI is among people with MS versus healthy controls. In preliminary results on the first 500 participants, presented at the annual meeting of the AAN in April, Dr. Zivadinov has found less prevalence of CCSVI among MS patients than did Dr. Zamboni. All of the participants in the Combined Transcranial and Extracranial Venous Doppler (CTEVD) Evaluation study underwent Doppler ultrasound scans to determine if they met the criteria for CCSVI. Out of the total, 56.4 percent of the participants with MS were found to have CCSVI, versus 22.4 percent of healthy controls. In Dr. Zamboni's 2009 study, 95 percent of the people with MS had some form of vein blockage or insufficiency. The conflicting results "raise a lot of questions," Dr. Miller says.

Even if the findings are mixed, I feel like anything that might help me is worth a try. I saw on the Web that I could go to Europe or India for vascular surgery to correct CCSVI. Is this a good idea?

The message from most of the participants in the Webinar was clear: Do not undergo invasive procedures designed to correct blood flow unless they are part of a well-designed clinical trial.

"These vascular procedures are associated with several potential, real, and serious complications—and need to be done by a qualified practitioner in a setting where we can learn whether the procedure has any beneficial impact on the disease process," says Dr. Corboy. "Only then will we learn if the procedure should be more generally used."

He points out that two Stanford University researchers who tried to use stents to correct CCSVI stopped their work after one patient developed a fatal hemorrhage and another suffered a complication in which the stent dislodged and required cardiac procedures to remove it.

Dr. Zamboni says that stents should not be used to treat CCSVI and agrees that the condition is best studied in clinical trials. But he adds that people with MS who are "rapidly declining" and have not responded to other treatment might want to ask their doctors for the treatment "on compassionate grounds."

How can I get information about participating in a clinical trial?

Dr. Zivadinov and his colleagues are proceeding with phase II of the CTEVD study. To find out more, contact the Buffalo Neuroimaging Analysis Center at 716-859-7040 or email ccsvi@bnac.net.

—Lisa A. Phillips

FRANK WRIGHT/ISTOCKPHOTO

ANSWERS ON P. 15

QUICK TIPS

Accessible Travel

When our son and his fiancée decided to get married in the summer at a ski resort in Northern California, 8,000 feet above sea level, we were awed by the beauty in the brochures. But as someone who has multiple sclerosis (MS) and uses a wheelchair, I was concerned about how the elevation would affect my health and ability to get around. I spoke with my doctor before going, and learned a few things along the way.

If you are a traveler with MS or another medical condition and are “going up in the world,” consider these tips for traveling to higher elevations and remote locations. My neurologist, Ivy Dreizin, M.D., collaborated with me to make sure this advice is useful and medically accurate:

- 1** If you have a chronic illness or medical condition, always consult your physician before planning a trip to higher altitudes.
- 2** Find out in advance about the availability of MS doctors or medical facilities nearby.
- 3** Keep a list of your medical contacts on hand in case a local doctor has to consult.
- 4** Jot down the phone numbers of local pharmacies in case you forget or lose your medication.
- 5** Before you make room reservations, ask if the hotel is wheelchair accessible. Accessibility standards vary from state to state: In general, newly constructed or recently remodeled build-



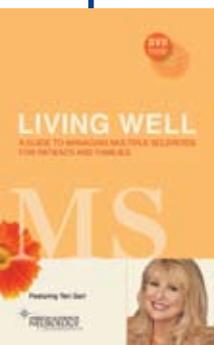
ings have the best facilities for disabled travelers; older motels or hotels may or may not be accessible.

- 6** To avoid altitude sickness (headache, nausea, dizziness), double the amount of water you drink several days before you leave. Continue to consume the increased amount during the trip.
- 7** When you are in higher elevations, your skin is exposed to more UV radiation. Apply sunscreen liberally throughout the day—even if it’s cloudy—and wear sunglasses.
- 8** Some cell phones may not work in mountainous areas, so check with your cell phone provider to see if they offer service where you’ll be staying. If they don’t, consider bringing walkie-talkies—you don’t want to be stranded in an isolated area, especially if you have limited mobility.
- 9** Be sure you have an emergency contact number should you need to summon help in the middle of the night. We were staying in condos that we rented during the summer “off season,” and there was no front desk after hours. One of the guests lost her key one night and had to bunk with another guest until the next day, when the condo management office opened up.
- 10** To make airline travel easier, consider shipping luggage ahead (by UPS or other service) to your destination. By sending gifts and bulky gear ahead, you can travel light and skip long waits at check-in counters and baggage claim. —Shelley Peterman Schwarz

NEUROLOGY NEWS

Just Diagnosed With Multiple Sclerosis?

Silver screen star Teri Garr is the host of the American Academy of Neurology Foundation’s newest patient-education video and guidebook, *Living Well: A Guide to Managing Multiple Sclerosis for Patients and Families*. The video and guidebook are aimed at answering important questions for newly diagnosed MS patients and their caregivers and can be viewed for free at aan.com/patients. A DVD and printed booklet can be ordered from aan.com/patients as well.



NEUROBICS ANSWERS CONTINUED FROM P. 11

1. LEFT SIDE: Starts with a letter in the first half of the alphabet. RIGHT SIDE: Starts with a letter in the second half of the alphabet.
2. LEFT SIDE: Contains the letter E. Right side: Does not contain the letter E.
3. LEFT SIDE: Two-syllable words. Right side: One-syllable words.