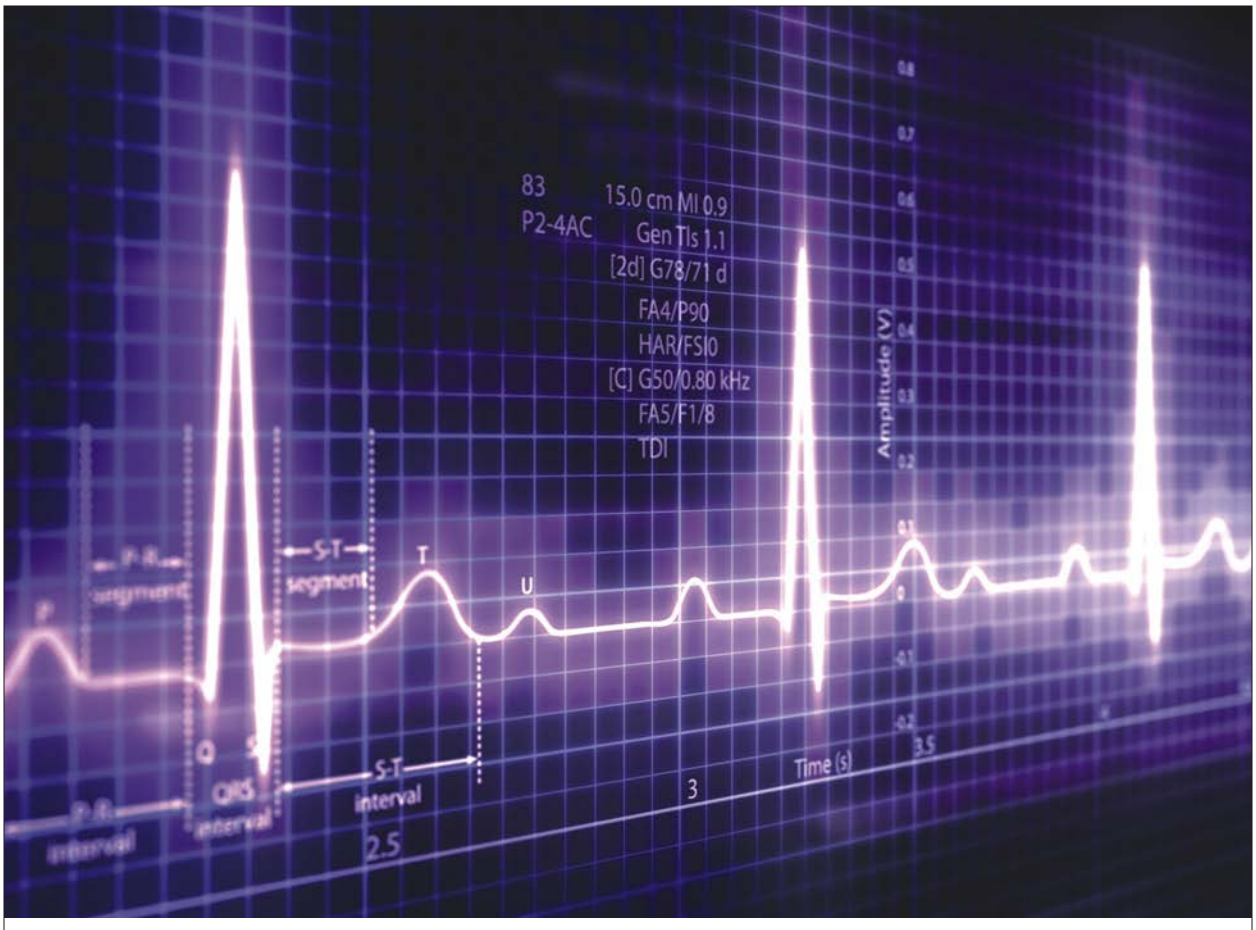

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SSRIs and Cardiovascular Health: Popular Antidepressants May Have Beneficial Side Effects for Cardiovascular Health

A class of antidepressants known as selective serotonin reuptake inhibitors (SSRIs) may provide a boost to cardiovascular health by affecting the way platelets, small cells in the blood involved in clotting, clump together, say researchers at the Loyola University Medical Center in Maywood, Ill.

In a study of 50 adults, the researchers found that platelets were slower to clump together, or aggregate, in participants who were taking an SSRI to treat depression. As depression is associated with an increased risk of cardiovascular disease, this finding could indicate a beneficial side effect for people who take SSRIs to treat depression, said Evangelos Litinas, MD, Research Associate in the Center's Pathology Department. Dr. Litinas is presenting the team's research at the American Physiological Society's annual Experimental Biology 2010 conference being held in Anaheim, CA from April 24-28.

SSRIs and Platelet Function SSRIs function to modulate the effect of serotonin in the brain. Neurotransmitters, like serotonin, are messages sent across the gap called the synapse between nerve cells in the brain. The cell sending the message, called the pre-synaptic cell, releases serotonin into the synapse. The serotonin is taken in by the receiving, post-synaptic cell, or be taken back by the pre-synaptic cell.

In a depressed patient, the post-synaptic cell doesn't take in enough serotonin and the message gets lost. To treat the depression, SSRIs decrease the ability of the pre-synaptic cell to reuptake the serotonin, leaving the message in the synapse longer and giving the post-synaptic cell a better chance of receiving the serotonin.

However, this blocking activity of SSRIs may have an effect on other cells in the body that require serotonin uptake. Small cells called platelets, which are involved in blood clotting, absorb serotonin only once and use it for their activation in response to injury.

When a blood vessel is injured in a healthy patient, their platelets are exposed to proteins that normally reside beneath the endothelium, the thin layer of cells lining blood vessel walls. These proteins activate the platelets and prompt them to send out finger-like projections that grab onto each other. This also activates the clotting system so that a clot will form at the wound site. This kind of platelet activation also occurs when blood vessel walls become inflamed in atherosclerosis "hardening of the arteries".

Once activated, the platelets release the contents of small packages that they carry called delta granules. These packages contain calcium, various energy-containing molecules, and serotonin. When the delta granules are released by activated platelets, the serotonin and other molecules work in the injured area to amplify the coagulation response.

However, Dr. Litinas and his team believe that in depressed patients who have an associated risk of cardiovascular problems, the blocking activity of SSRIs may have a side-effect of preventing the serotonin uptake by platelets, making them less responsive to aggregation and may thereby improving the patients' cardiovascular health.

To test their hypothesis, the researchers recruited 50 volunteers, 25 who were healthy and were not taking antidepressant medications and 25 who were being treated for depression with an SSRI. The team collected blood samples from each volunteer at the beginning of the protocol and again at the study's fourth week and eighth week. After each round of blood-drawing, the team separated the blood into its components to obtain the platelet-rich plasma for study.

The researchers then treated all of the samples with platelet-activating substances and with saline, which does not activate platelets. They observed platelet activity and

quantified the amount of aggregation in each sample by using an aggregometer, a machine that aims light into liquid samples. Cells that do not aggregate tend to prevent light from getting all the way through a sample to the other side, whereas cells that aggregate form large clusters that sink down out of the way, allowing the light to shine through.

When the platelets from healthy volunteers were treated with platelet-activating substances at the 4-week time point, 95% of the cells aggregated. In contrast, the platelets of participants taking an SSRI showed only 37% aggregation, indicating that the SSRI had somehow inhibited or changed the platelets' ability to clump together.

As the study progressed, the researchers noticed something peculiar: The platelets taken from SSRI-treated patients at the 8-week mark aggregated more than those drawn at the 4-week mark. This suggested that SSRIs have the greatest impact on preventing platelet activation early on in treatment. Dr. Litinas and his team believe this may be because the body takes several weeks to start modulating SSRIs in the body. The team has extended the study to include samples drawn at the 12-week mark. They will also conduct a study using another brand of SSRI.

"The reason we're doing this is to better the lives of depressed patients," said Dr. Litinas. "There is clear evidence that depressed patients have a higher risk of cardiovascular disease, and we want to eliminate that. Since depression can be treated with an SSRI, maybe the cardiovascular disease risk can also be decreased. We want our patients to live longer and happier lives, without depression or the risk of heart problems."

Dr. Litinas' colleagues for this study are Dr. Jawed Fareed and Dr. Omer Iqbal, both of whom are affiliated with the Department of Pathology, Loyola University Medical Center, Maywood, IL; and Erin Tobin, Dr. John Piletz, Dr. Edwin Meresh, and Dr. Angelos Halaris, all of the Department of Psychiatry, Loyola University Medical Center.