Understanding the role of an omega-3 fatty acid in the prevention of arrhythmias

August 15 2024

While omega-3 polyunsaturated fatty acids are easily available as supplements, their protective effects against cardiac diseases like arrythmia, are not fully understood. A study by researchers from Japan has now revealed that one such compound, named eicosapentaenoic acid, helps regulate the expression of calcium ion channels in heart muscle cells, which are often dysregulated in diets rich in saturated fats. Credit: Jernej Furman from Slovenia

Over the past few decades, scientists have generated a pile of evidence suggesting that a diet rich in saturated fats is enough to cause heart diseases. Besides other problems like diabetes and atherosclerosis, saturated fats have also been linked to life-threatening arrhythmias.

Interestingly, based on animal and human studies, certain omega-3 polyunsaturated fatty acids seem to have beneficial effects on cardiovascular health. In particular, eicosapentaenoic acid (EPA), which is found in fish oil, not only has vasodilator and antiplatelet effects, but can even help prevent atrial fibrillation and other arrhythmias. Despite EPA being readily available as a dietary supplement, the effect of EPA on cardiomyocytes and their underlying mechanisms of action are not fully understood.

In a recent study published online on July 10, 2024 in the *International Journal of Molecular Sciences*, a research team from Japan set out to bridge this knowledge gap. Led by Associate Professor Masaki Morishima from Kindai University, they investigated the role of EPA in inducing long-term electrical changes in cultured mouse cardiomyocytes using a variety of bioanalytical techniques. Their research article was co-authored by Dr. Katsushige Ono from Oita University and Dr. Kazuki Horikawa from Tokushima University.

The main focus of this work was on how an oleic acid/palmitic acid mixture (OAPA), two well-studied saturated fats, impact calcium homeostasis in cardiomyocytes by affecting Ca^{2+} ion channels, and whether EPA can rescue these changes and restore normal functioning.

First, using real-time PCR, the researchers found that OAPA markedly reduced the mRNA levels of Cav1.2 L-type Ca^{2+} channels. Live cell imaging systems confirmed that OAPA also lowered the spontaneous beating rate of cardiomyocytes.

Notably, these changes were prevented when even a small amount of EPA was applied together with OAPA, rescuing both mRNA and protein expression levels of Cav1.2. Through electrophysiological measurements, the researchers also confirmed that the reduction in Cav1.2 channel current caused by OAPA was also prevented by EPA.

To gain more detailed insights into the effects of OAPA and EPA, the team then focused on a transcription factor known as cAMP response element binding protein (CREB), whose phosphorylation serves as an index of Cav1.2 transcription. While OAPA reduced CREB mRNA in a way entirely consistent with changes in Cav1.2 mRNA, EPA was able to prevent these alterations.

The researchers then turned their attention to FFAR4, an EPA receptor. Interestingly, the researchers observed that an agonist to FFAR4, mimicking the effects of EPA rescued the changes caused by OAPA, whereas an antagonist to FFAR4 outright blocked the effects of EPA. Together, these findings reveal that EPA is involved in a regulatory pathway mediated by FFAR4 that affects the regulation of L-type Ca^{2+} channels in cardiomyocytes.

A final set of experiments revealed that OAPA was responsible for oxidative stress through the accumulation of reactive oxygen species (ROS). Again, EPA could rescue ROS accumulation induced by OAPA. However, it turns outs that ROS accumulation affects the transcription of Cav1.2 L-type Ca^{2+} channels through yet another pathway that is independent of FFAR4.

Put together, this study has shed some much needed light on the underlying mechanisms by which EPA could bolster heart health.

"Although there are techniques and drugs to control arrhythmias, methods to prevent them have not been established," remarks Dr.

Morishima.

Adding further, she states, "The results of our study suggest that EPA has a protective effect on cardiomyocytes by normalizing abnormalities caused by the intake of excessive amounts of saturated fatty acids, which occurs in high-fat diets."

The team envisions that these findings will pave the way for smarter dietary choices and new health guidelines. "While research on nutrients and disease prevention can take a long time, studies like ours lay the groundwork for practical nutritional strategies that could seamlessly fit into everyday diet," concludes Dr. Morishima, hoping for a healthier future.

More information: Masaki Morishima et al, Eicosapentaenoic Acid Rescues Cav1.2-L-Type Ca2+ Channel Decline Caused by Saturated Fatty Acids via Both Free Fatty Acid Receptor 4-Dependent and -Independent Pathways in Cardiomyocytes, *International Journal of Molecular Sciences* (2024). DOI: 10.3390/ijms25147570

Provided by Kindai University