Molecular hub links obesity, heart disease to high blood pressure

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(Medical Xpress)—Obesity, heart disease, and high blood pressure (hypertension) are all related, but understanding the molecular pathways that underlie cause and effect is complicated.

A new University of Iowa study identifies a protein within certain brain cells as a communications hub for controlling blood pressure, and suggests that abnormal activation of this protein may be a mechanism that links cardiovascular disease and obesity to elevated blood pressure.

"Cardiovascular diseases are the leading cause of death worldwide, and hypertension is a major cardiovascular risk factor," says Kamal Rahmouni, Ph.D., UI associate professor of pharmacology and internal medicine, and senior study author. "Our study identifies the protein called mTORC1 in the hypothalamus as a key player in the control of blood pressure. Targeting mTORC1 pathways may, therefore, be a promising strategy for the management of cardiovascular risk factors."

The hypothalamus is a small region of the brain that is responsible for maintaining normal function for numerous bodily processes, including blood pressure, body temperature, and glucose levels. Signaling of mTORC1 protein in the hypothalamus has previously been shown to affect food intake and body weight.

The new study, which was published April 2 in the journal *Cell Metabolism*, shows that the mTORC1 protein is activated by small molecules and hormones that are associated with obesity and cardiovascular disease, and this activation leads to dramatic increases in blood pressure.

Leucine is an amino acid that we get from food, which is known to activate mTORC1. The UI researchers showed that activating mTORC1 in rat brains with leucine increased activity in the nerves that connect the brain to the kidney, an important organ in blood pressure control. The increased nerve activity was accompanied by a rise in blood pressure. Conversely, blocking this mTORC1 activation significantly blunted leucine's blood pressure-raising effect.

This finding may have direct clinical relevance as elevated levels of leucine have been correlated with an increased risk of high blood pressure in patients with cardiovascular disease.

"Our new study suggests a mechanism by which leucine in the bloodstream might increase blood pressure," Rahmouni says.

Previous work has also suggested that mTORC1 is a signaling hub for leptin, a hormone produced by fat cells, which has been implicated in obesity-related hypertension.

Rahmouni and his colleagues showed that leptin activates mTORC1 in a specific part of the hypothalamus causing increased nerve activity and a rise in blood pressure. These effects are blocked by inhibiting activation of mTORC1.

"Our study shows that when this protein is either activated or inhibited in a very specific manner, it can cause dramatic changes in blood pressure," Rahmouni says. "Given the importance of this protein for the control of blood pressure, any abnormality in its activity might explain the hypertension associated with certain conditions like obesity and cardiovascular disease."

Rahmouni and his team hope that uncovering the details of the pathways linking mTORC1 activation and high blood pressure might lead to better treatments for high blood pressure in patients with cardiovascular disease and obesity.

More information:
www.cell.com/cell-metabolism/abstract/S1550-4131%2813%2900095-8

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