

Limiting protein or certain amino acids before surgery may reduce risk of surgical complications

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Limiting certain essential nutrients for several days before surgery—either protein or amino acids—may reduce the risk of serious surgical complications such as heart attack or stroke, according to a new Harvard School of Public Health (HSPH) study.

The study appears in the January 25, 2012 issue of [Science Translational Medicine](#).

"Food restriction as a way to increase stress resistance may seem counterintuitive, but in fact our data indicate that the well-fed state is the one more susceptible to this kind of injury," said James Mitchell, assistant professor of genetics and complex diseases at HSPH.

The researchers, led by Mitchell and Wei Peng, a former HSPH postdoctoral fellow, analyzed two groups of mice. One group was allowed to eat normally for 6 to 14 days; the other group was given a diet free of protein or lacking a single amino acid ([amino acids](#) are the building blocks of proteins). Both groups were then subjected to surgical stress that could potentially harm the kidneys or liver. In the mice that were allowed to eat as usual, about 40 percent died. The protein- and amino acid-free mice all survived.

The researchers also found that removing the gene that senses levels of any type of amino acid eliminated the protective effect. This suggests

that the pathway activated by amino acid deficiency—rather than the absence of any particular amino acid—is responsible for the observed benefits, and opens up the potential for targeting drugs toward that pathway.

The results are significant because they pinpoint protein as an important substance to eliminate from the diet before surgery to avoid complications. Stroke risk related to cardiovascular surgery ranges from 0.8% to 9.7%, depending on the procedure. Heart attack risk is 3% to 4%.

In numerous animal studies over the past few decades, scientists have found that long-term dietary restriction can improve health and lengthen life. Benefits include increased stress resistance, reduced inflammation, improved blood sugar regulation, and better cardiovascular health—and many of these benefits extend to humans. There is debate, however, about whether the benefits stem from the source of the calories (fat, sugar, or protein) or simply the total calories. Recent research on fruit flies demonstrated the benefits of restricting protein. The HSPH study aimed to provide further clarity by determining the benefits of protein or amino acid restriction in rodents.

As a next step, Mitchell and his colleagues will try to determine whether dietary preconditioning works as well lowering surgery-related risk in humans as it did in mice. They have taken early planning steps with colleagues at Brigham and Women's Hospital in Boston on a clinical trial of patients on protein-free diets before surgery. If the benefits are confirmed in humans, it may be possible to perform surgeries with significantly reduced risk of complications.

More information: "Surgical Stress Resistance Induced by Single Amino Acid Deprivation Requires Gcn2 in Mice," Wei Peng, Lauren Robertson, Jordan Gallinetti, Pedro Mejia, Sarah Vose, Allison Charlip,

Timothy Chu, James R. Mitchell. *Science Translational Medicine*, online January 25, 2012.

Provided by Harvard School of Public Health

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