A proposed link between aging, autism, and oxidation

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Professor Richard Deth's research on methionine synthase was recently published in the journal PLOS ONE. Credit: Richard Deth

Like any factory, the body burns oxygen to get energy for its various needs. As a result, detrimental byproducts are released and our cells try to clean up shop with antioxidants. But as we age, this process becomes a losing battle.

"Oxidation inexorably moves us along toward an oxidized state," said pharmaceutical sciences professor Richard Deth. "You have to deal with it progressively."

One option is to slow down the synthesis of new proteins, a process that requires energy. Indeed, as we age, we produce fewer new proteins, which explains why our capacity for learning and healing suffer as we grow old.

Since every protein originates from instructions in the DNA, protein synthesis can be slowed down by turning off particular genes. A process called epigenetic regulation accomplishes the task by adding molecular tags on top of the genome. The protein methionine synthase regulates this process. But what regulates methionine synthase? Oxidation.

"This enzyme is the most easily oxidized molecule in the body," said Deth, whose research on the subject was recently published in the journal PLOS ONE. The senior author for the study, Christina Muratore, received her doctorate in pharmaceutical sciences from Northeastern in 2010.

Whenever the body is under oxidative stress, Deth explained, methionine synthase, or MS, stops working. He and his team hypothesized that MS plays an important regulatory role in aging and that it might be impaired in autism, which Deth has connected to unchecked oxidative stress in previous research.

To examine their hypothesis, the researchers looked at postmortem human brain samples across the lifespan, with subjects as young as 28 weeks of fetal development to as old as 84 years. They measured the levels of a molecule called MS mRNA, which transcribes the genetic code for methionine synthase into actual protein.

As the subjects aged, their brain tissue showed lower levels of MS mRNA. But, surprisingly, the levels of the protein itself remained constant across the lifespan.

Deth and his colleagues suspect that this observed decrease in MS mRNA over our lives may act as a check in the system to save energy that we no longer have in plentiful supply and to slow down oxidative stress. "One way that the system can guard against too much protein synthesis is to restrict the amount of mRNA," Deth said.

The team also compared MS protein and mRNA levels between brain tissue samples from autistic and normally developing subjects. Autistic brains had markedly less MS mRNA than the control samples but similar protein levels. Additionally, the age-dependent trend seen in normally developing brains was not mimicked among the autistic sample.

If decreased MS mRNA does mean decreased protein production, it's no big deal for adults who don't need to make new proteins as often. But for the developing brain, new proteins are critical. "Your capacity for learning might be prematurely reduced because metabolically you can't afford it," Deth suggested.

While the results are preliminary and will benefit from repeated studies and more investigation, Deth's findings add to a growing body of evidence linking both aging and autism to oxidative stress.

More information: www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0056927

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