CoQ10 and Minocycline not helpful in Mouse Model

CHDI scientists and their colleagues at Psychogenics have conducted a rigorous mouse study and found that neither CoQ10 nor minocycline were helpful in the R6/2 mouse and that high doses of minocycline resulted in decreased survival time.

CHDI contracted with Psychogenics to carry out studies of promising compounds in mouse models of Huntington's Disease, including compounds that had already been reported as helpful. The mice are housed in better conditions with better and more accessible food. The studies involve larger numbers of mice, matched control and experimental groups, semi-randomly selected, assessment on several behavioral measures, and real rather than estimated survival time data.

CoQ10 had been previously reported as helpful in a mouse model of HD. A Phase III clinical trial which ended in 2001 found a modest trend in slowing disease progression but it did not reach statistical significance. The rationale behind the interest in CoQ10 is that it may boost cellular energy, known to be impaired in Huntington's Disease and it is an antioxidant. Oxidative stress is also believed to be a problem in the disease.

What accounts for the difference between the findings in this study and previous studies? Why did a promising compound fail to help the mice? There are a number of possibilities. One likely possibility concerns bioavailability. CoQ10 has poor bioavailability in the brain and it may be that sufficient levels weren't achieved in the brain. On the other hand, supplementation can help raise levels in the brain if they are too low because of poor nutrition. If the mice in the previous studies were nutritionally deprived as compared to those in the current study, this may explain why supplementation did help them. The question of whether an analogue of CoQ10 with better bioavailability might help the HD mice and Huntington's patients is still an open question.

Another possibility is that the enriched housing addresses the energy deficiency to the extent that CoQ10 cannot add additional effects.

Studies with minocycline have had mixed results. Some studies with the R6/2 mice found it to be helpful but others did not. Minocycline did not help the N171-82Q model and actually was toxic in the 3NP mouse model. A clinical trial of higher dose minocycline in ALS patients found that the minocycline group died sooner than those in the treatment group but a lower dose trial in HD patients found no safety issues although the results did not warrant pursuing it as a treatment.

The initial interest in monocline was because it was hoped that it would prevent apoptosis, programmed cell death. Later researchers were interested in the antibiotic's possible effect on neuroinflammation, free radical damage, excitotoxicity, and aggregation.

In this study, a small dose was injected in one experimental group and two higher doses were administered in food to two additional experimental groups. In the first group, there were statistically significant improvements in body weight and two behavioral measures; however they did not persist and there was no improvement in survival time. In the higher dose groups, no improvements were found and survival time was decreased.

The authors also note that there is a publishing bias in that studies with good results are more likely to be published than studies that find a drug or supplement to be ineffective. The standard of statistical significance is that it should be no more likely than one in twenty that the results are due just to chance rather than being meaningful. If twenty studies of possible treatments are carried out, the chances are good that that one of them might have a statistically significant result just due to random differences between the two groups rather than treatment effects. If disappointing results are not made publicly available, we won't know if something has been tried before and it exaggerates the importance of achieving one. The authors call for a public forum to make the results of all these studies known regardless of whether an academic journal has an interest in publishing them

Reference:

Liliana B. Menalled, Monica Patry, Natalie Ragland, Phillip A. S. Lowden, Jennifer Goodman, Jennie Minnich, Benjamin Zahasky, Larry Park, Janet Leeds, David Howland, Ethan Signer, Allan J. Tobin, and Daniela Brunner. **"Comprehensive Behavioral Testing in the R6/2 Mouse Model of Huntington's Disease Shows No Benefit from CoQ10 or Minocycline."** PLoS One. 2010 Mar 22;5(3):e9793.

- *Marsha L. Miller, Ph.D., April 26, 2010*