

## **Weight loss in Huntington's Disease**

Weight loss is a characteristic symptom in Huntington's Disease and also a clue to unraveling its mysteries. European researchers followed 517 early stage HD patients for three years and found that weight loss was significant overall and positively correlated with the CAG count. In other words, the higher the number of CAG repeats, the faster weight loss occurred.

What accounts for this weight loss? Of course, as the disease progresses and swallowing becomes more difficult, there may be a decreased intake of calories, contributing to weight loss. But this study shows that weight loss actually occurs early on in HD patients just as it does in the R6/2 mice, before there is any decrease in caloric intake. The researchers didn't collect information about caloric intake in their patients, but we know that as weight loss occurs, patients and their families will work on increasing calories to get weight back to normal. The HD mice have also been found to increase their caloric intake.

Could the decrease be a result of increased movements? Chorea does use up additional calories. However, weight loss was not correlated with the total motor score on the United Huntington's Disease Rating Scale (UHDRS) and chorea does not correlate with the CAG count.

What about medication? Neuroleptic use can cause changes in energy homeostasis but patients taking neuroleptics were excluded from this study.

The patients studied were in the clinical trial for riluzole. However, the trial showed that riluzole did not affect clinical outcome; in other words, it is not an effective treatment for HD. The researchers also confirmed that riluzole use does not affect weight loss.

It appears then that Huntington's Disease causes a metabolic problem. This study builds on earlier research by Coaliton for the Cure researcher Marcy MacDonald and colleagues who were working with cell models and a knock in mouse model. They showed that CAG counts are negatively correlated with mitochondrial energy production. The higher the number of CAG repeats, the less energy is produced to power the cell.

This research is encouraging because it shows that work with cell and animal models can yield insights that are confirmed in human HD patients. It also suggests that attempts to boost energy metabolism may result in treatments for the disease. Two supplements that boost energy, creatine and CoQ10, and are now in Phase III clinical trials.

## **References**

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- *Marsha L. Miller, Ph.D., December 22, 2008*