Exercise Found Harmful in a Mouse Model

People at risk for Huntington's Disease are interested in research which suggests how to live a healthy lifestyle that postpones disease onset as long as possible. One of the most common recommendations and the most solidly researched has been exercising to fitness. There are two reasons for this. The first is that the overall health benefits to the general population are widely known. Exercise leads to cardiovascular fitness but in addition has been shown to improve memory, ameliorate depression, delay the cognitive deficits of aging, and reduce the likelihood of neurodegeneration (Cottman 2007). It makes sense that those who are healthier will do better when confronted with a disease. The second is that exercise is known to boost Brain Derived Neurotrophic Factor (BDNF), a protein associated with the generation and protection of neurons. BDNF is reduced in the brains of HD patients.

A new study from researchers at the National Institute of Health has examined the effects of exercise on a mouse model of Huntington's Disease and found that exercise had numerous negative effects on the mice (Potter 2010). The researchers worked with male N171-82Q mice and found that those mice housed with a running wheel became symptomatic earlier, had more severe motor impairments and a greater reduction in striatal volume than the HD mice that did not have the opportunity for voluntary running. In addition, exercise did not bring about improvement in cognition, hypoglycemia, or hippocampal neurogenesis.

Earlier studies with R6/1 and R6/2 mice showed that exercise conveyed some benefits though not as much as environmental enrichment (Van Dellen 2008, Cepeda 2010). In the R6/1 mice, exercise was found to delay several motor symptoms. In the R6/2 mice, exercise prevented the reduction in striatal medium-sized spiny neuron membrane capacitance (the ability to hold an electric charge). The current study is the first to find a negative effect from exercise on a mouse model.

What does this mean for Huntington's Disease patients and those at risk? The authors conclude that the recommendation for exercise should be revisited. In addition to their research findings they cite a case study where a marathon runner with a CAG count of 41 had a sooner than expected disease onset. However, one case is not convincing given the wide range of age of onset for any CAG count and the existence of modifying genes as well as environmental factors which make prediction at the individual level impossible. Other runners have had different outcomes. For example, I am well acquainted with a

long time marathon runner with a CAG count of 40 who is symptom free at 64. It is not possible to conclude that the first runner had an earlier onset because of exercise nor that the second has a later onset for the same reason. A much larger study of marathon runners would be needed to begin to draw conclusions.

Still, the study raises an important question. Do these finding translate from mice to people? We know from research conducted by Marcy MacDonald and colleagues that cellular energy is negatively correlated with CAG counts; that is, the higher the CAG count, the lower the amount of energy that is being produced in the cell. The mouse models have high CAG counts; in this study the mice have 82 repeats. The average person with Huntington's Disease has fewer than 50 counts. Counts for Juvenile HD are usually much higher. It may be that with very high CAG counts, the demands placed on the cell by exercise cause more damage than any benefits that might accrue. However, it is also possible that the equation might be different for the lower CAG counts seen in adult onset HD.

References:

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