

Sertaline Helps Two Mouse Models of HD

Coalition for the Cure researcher Christopher Ross and his colleagues have shown that the SSRI antidepressant sertaline (Zoloft) extends survival time in two mouse models of HD, the R6/2 mouse and the N181-82Q mouse.

SSRI stands for selective serotonin reuptake inhibitor. These antidepressants are commonly prescribed for depression in Huntington's Disease patients. Both mouse models have a fragment of the human HD gene with the expanded CAG repeats inserted into their genetic code.

The HD mice who received sertaline did better than their untreated counterparts with increased survival time, improved rotarod performance (a motor measure), and reduced brain atrophy. Body weight was not improved and inclusions (protein aggregates which are associated with the disease) were not reduced.

Sertaline also increased levels of brain derived neurotrophic factor (BDNF). The expression of BDNF is known to be reduced in Huntington's Disease. BDNF is associated with both the protection of neurons and the growth of new ones (neurogenesis). Neurogenesis was increased in the sertaline treated mice.

To see if neurogenesis was a significant factor in the positive results, the researchers blocked neurogenesis with X rays in sertaline treated mice. Motor performance failed to improve and the extension of survival time, although it did occur, was not as great. This showed that increased neurogenesis is a major factor in the beneficial effect of sertaline.

The positive results are consistent with earlier studies that found that two other SSRIs, fluoxetine (Prozac) and paroxetine (Paxil), were helpful in mouse models.

Sertaline appears to be another good candidate for the therapeutic pipeline. It is helpful in two different mouse models, it is an FDA approved drug for depression, and it can be taken long term with minimal side effects. Further, the levels needed to be effective in the mice are comparable to human dosages. It did not improve all of the symptoms nor restore the health of the mice, but the improvements were significant. This suggests that, if comparable results were to be obtained in HD patients, sertaline would be a good component in a cocktail of treatments.

References

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- *Marsha L. Miller, Ph.D., June 25, 2008.*