



Sertoli Cell Grafts for Huntington's Disease. An Opinion.

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The role of inflammation in CNS diseases is controversial, but growing evidence suggests that anti-inflammatory agents can minimize and/or prevent neural degeneration and its associated behavioral consequences. Sertoli cells can be grafted into the CNS to locally deliver molecules with known trophic and anti-inflammatory effects on the surrounding tissue. When Sertoli cells are grafted into the 3-nitropropionic acid (3-NP) model of Huntington's disease the protective effects are quite similar to those obtained using systemic treatments with NSAIDs (Salzberg-Benhouse *et al.*, *J. Pharmacol. Exp. Ther.* 306:218-228, 2003). While these data alone do not provide unequivocal support for the notion that Sertoli cell grafts exert their beneficial effects via modulating local inflammation, they do provide an interesting convergence between data sets. The benefits of Sertoli cell grafts should be more thoroughly examined in animal models of inflammation.

I recently read with great interest the article by Rodriguez *et al.*, entitled "Effects of Sertoli cell transplants in a 3-nitropropionic acid model of early Huntington's disease: a preliminary study" (Rodriguez *et al.*, 2003). The authors describe the interesting finding that Sertoli cells, when transplanted into the striatum, are able to normalize the behavioral consequences of the 3-nitropropionic acid (3-NP) lesion. Interestingly, this same group had previously reported significant decreases in the local tissue reaction surrounding grafts of Sertoli cells under similar circumstances. Whether this represents a diminished response to the initial surgical trauma via the secretion of protective growth factors from the Sertoli cells, a dimin-

ished immunologic/inflammatory response, or a combination of the two remains to be determined. But what is fascinating is how these data (and other data from studies grafting Sertoli cells and islets) dovetail with our own recent findings about the utility of anti-inflammatory agents in models of Huntington's disease. We reported that systemic treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) such as flurbiprofen and *N*-[2-(cyclohexyloxy)-4-nitrophenyl]-methanesulfonamide (NS-398) exerted a very powerful protection of striatal neurons in the quinolinic acid model of Huntington's disease (Salzberg-Benhouse *et al.*, 2003). Dose-dependant decreases in lesion volume correlated with significant improvements in motor function suggesting that the anti-inflammatory effects of cyclooxygenase-2 (COX-2) inhibition protect neurons from neurodegeneration. Sertoli cells act as biofactories for numerous neurotrophic factors, but they are also secretors of potent anti-inflammatory agents. While the role of inflammation in Huntington's disease is speculative, it is worthwhile theorizing about the therapeutic potential of compounds or cells that act in this way. This is certainly a complicated issue but fertile enough to warrant a little excavating around an under-appreciated potential of Sertoli cells.

References

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