

### **GSH, Dopamine and Glutamate: Roles in Parkinson's Disease.**

GSH is utilized by the granular storage system of dopamine in PC12 pheochromocytoma cells and it is likely that GSH protects susceptible parts of the granular transport system against (possibly dopamine-induced) oxidative damage.<sup>63</sup> In PC12 and C6 glial cell lines, glutamate toxicity causes oxidative stress and GSH depletion by reducing cystine uptake and results in apoptotic cell death.<sup>64, 65</sup>

These research models of Parkinson's disease suggest a key role for GSH in glutamate excitotoxicity. Strategies designed to maintain GSH levels protect against glutamate and prevent dopamine-induced cell death and have enhanced neuronal survival.<sup>66,67</sup>

Astrocyte mediation of enhanced neuronal survival is abolished by GSH deficiency.<sup>68</sup> The neuroprotective role of astrocytes involves a number of activities: expression of antioxidant enzymes, transport and metabolism of glucose that yields reducing equivalents for antioxidant regeneration and lactate for neuronal metabolism, synthesis of GSH, and recycling of vitamin C.<sup>69</sup> Many of these functions require GSH or cystine.

Astrocytes, like macrophages, prefer cystine and glutamate for GSH synthesis<sup>70,71</sup> whereas; cysteine and glutamine are preferred by neurons. These differential preferences allow astrocytes to regulate neuronal GSH.<sup>68</sup>

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