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PCB-Induced Neurotoxicity in Organotypic Co-Cultures of Developing Rat Substantia Nigra and Striatum

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Polychlorinated biphenyls (PCBs) are persistent environmental contaminants that are toxic to both the adult and developing nervous system, especially affecting dopamine (DA) function. In order to characterize the effects of PCB-induced neurotoxicity on basal ganglia function we employed an organotypic co-culture system of developing rat substantia nigra (SN) and striatum to model the developing nigro-striatal DA system. The organotypic co-culture system provides an excellent model to examine the temporal relationship of neurotoxic events occurring in the basal ganglia following exposure to an environmentally relevant mixture of PCBs. Co-culture PCB exposure resulted in reductions in tissue DA concentrations and increased neuronal cell death in both the SN and striatum. Additionally, PCB exposure reduced the number of DA neurons in the SN compared to vehicle control. These neurotoxic effects were observed in the SN prior to any measurable changes in the striatum. Furthermore, there was an increase in overall neuronal cell death prior to a reduction in the number of SN DA neurons, which we hypothesize is the death of GABAergic neurons in both the SN and striatum. Susceptibility of GABAergic neurons to PCB-induced toxicity is supported by Western Blot analysis showing reductions in glutamic acid decarboxylase (GAD) protein content. These results will aid in understanding the role that developmental exposure to PCBs has on the nigro-striatal DA system, and has important implications for disease states such as Parkinson's disease. Supported in part by NIH grant 1P01ES11263-01 and EPA grant R-82939001.