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Effects of PCB Congeners in Rodent Neuronal Cells in Culture

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We attempted to analyze the mechanism of polychlorinated biphenyl (PCB)-induced neurotoxicity and identify the target molecules in the neuronal cells for PCBs. Since the developing neuron is particularly sensitive to PCB-induced neurotoxicity, we isolated cerebellar granule cells derived from 7-day old Sprague Dawley (SD) rats and grew cells in culture for additional 7 days to mimic PND-14 conditions. Only non-coplanar PCBs at a high dose showed a significant increase of total protein kinase C (PKC) activity at phobol 12,13-dibutyrate ([^{3}H]PDBu) binding assay, indicating that non-coplanar PCBs are more neuroactive than coplanar PCBs in neuronal cells. PKC isozymes were immunoblotted with the selected monoclonal antibodies. PKC-α, δ and ε were activated with non-coplanar PCB exposure. Receptor for activated C kinase-1 (RACK-1), anchoring protein for activated PKC, was more induced with exposure to coplanar PCBs than non-coplanar PCBs. Reverse transcription PCR (RT-PCR) analysis showed induction of neurogranin (RC-3) and growth associated protein-43 (GAP-43) mRNA with non-coplanar PCBs. The results indicate that these factors may be useful biomarkers for differentiating non-coplanar PCBs from coplanar PCBs. The present study demonstrated that non-coplanar PCBs are more neuroactive congeners than coplanar PCBs.

Keyword: PCB, neurotoxicity, Structure-activity relation, cerebellum, PKC