Cell death mechanisms activated by polychlorinated biphenyls in neural stem cells with special focus on mitochondrial functions

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With globalization and mass awareness, there is a growing concern of environmental pollutants and contaminants released in to the environment where they are taken up by plants, animals, and humans. Polychlorinated biphenyls (PCBs) are one of these pollutants, which although banned in the 1970s due to their alleged carcinogenic nature, still pose a threat to human health. Firefighters and workers who cleaned up debris at Ground zero after the 9/11-2001 incident in New York were exposed to PCBs along with different toxicants by air and skin contact. Reports state that after this incident, 130 000 gallons of transformer oil containing PCBs along with other environmental pollutants seeped into the ground, resulting in an increase of PCB levels to 75 000 times the normal values. On the whole, we are much at risk of exposure and it is therefore necessary to study the effects of PCBs in humans, especially their effects on target organs such as the nervous system. Animal studies have shown that PCBs induce various neurobehavioural alterations in mice and epidemiological studies indicate neuropsychological deficits in children exposed to PCBs. These studies clearly indicate that PCBs affects the developing nervous system. Research in my group has focused our investigation on the effect of PCBs on neural stem cells (NSCs) since they constitute a major part of the developing brain. Hence, they are a good model system for cellular toxicity studies during early brain development.

Mitochondria are the energy factories of the cells. The main aim of the study was to elucidate the possible effects of PCBs on mitochondrial functions in neural stem cells (NSCs) by combining different assays, such as cellular ATP levels, mitochondrial respiration and the flow of calcium in mitochondria, important in its energy metabolism. In the literature, PCBs have been founbd to affect the integrity of mitochondria as well as to disrupt calcium flow and cellular signaling. They have also been shown to decrease cellular respiration and energy production (ATP synthesis).

Results show a decrease in mitochondrial respiration and cellular ATP levels in NSCs exposed to various PCBs, which indicates that PCBs disrupt the mitochondrial function. I could also see disruption in mitochondrial calcium flow that indicated damage to the mitochondrial membrane integrity, which led to cell death. Overall, the data concur with previous studies reporting that PCBs cause damage to mitochondrial membranes and decrease ATP synthesis, resulting in the release of mitochondrial proteins and the formation of reactive oxygen species that in the end can lead to cell death.

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